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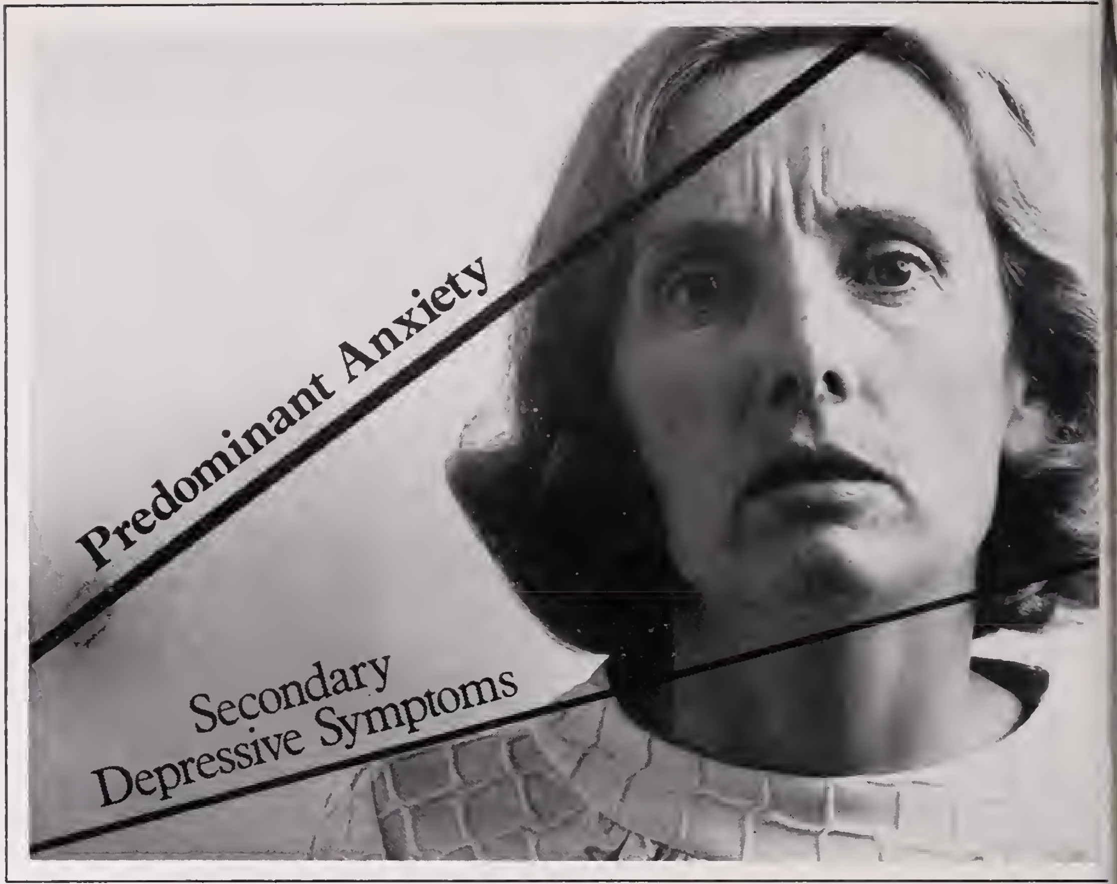
"Winter Wonderland"

John E. Lonstein, M.D.



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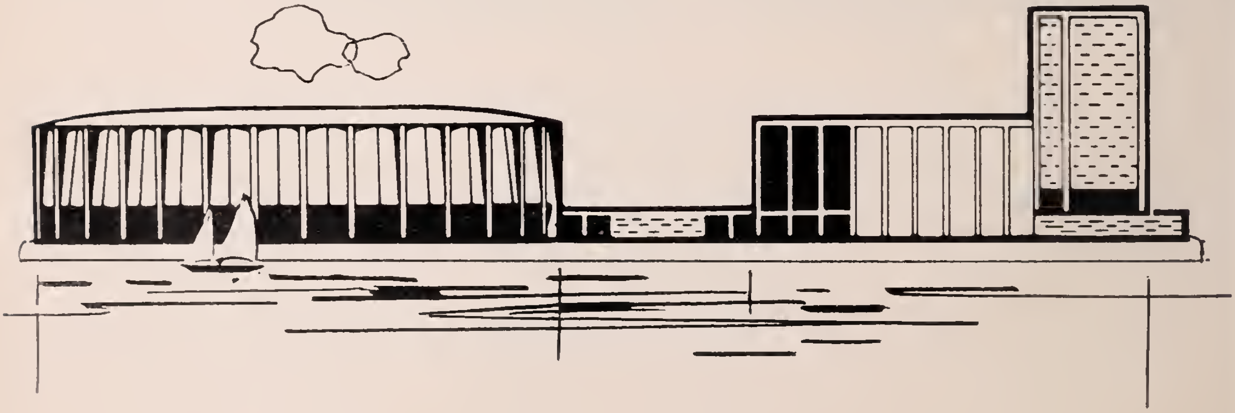

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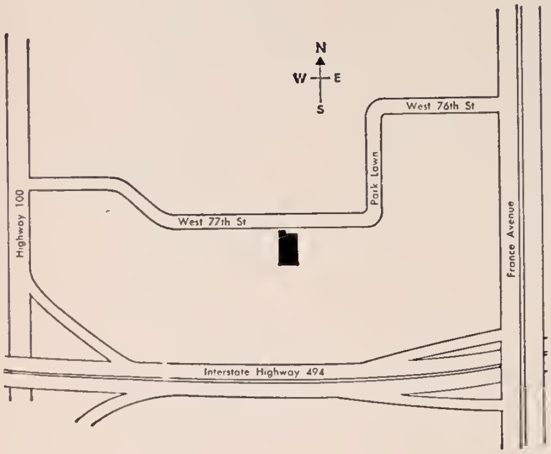

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President's Letter

Health Planning

My romance with the airlines of America is a mixed one and my feelings about the industry, ambivalent. While I appreciate the rapid safe transport from one part of the world to another, I often deplore the small things that have to do with running an airline. The other evening coming home from Milwaukee one of the young ladies managed with admirable dexterity to spill half of someone's unfinished martini all over my best gray suit and my Countess Mara tie which was a Christmas gift from someone (thank goodness it wasn't a Bloody Mary). On another airline while the trays were being served, one of the young ladies committed an incredible social (and hygienic) blunder. It seems my lot to be witness to ineptitude, negligence, error and carelessness on the part of agents of this great industry. Although I have grown to regard myself an expert in their errors to the point of having developed skill in assessing from without, all of this expertise is in the face of my utter ignorance of the anguish and problems and difficulties that must be part of a great system and the undeniable fact that the airlines have evolved an efficient and safe system of transporting masses of people around the globe. In spite of my self-designated authority in this industry I haven't earned even my private pilot's license.

A like expertise from without is chipping away at our medical delivery system these days. Medical planning appears to be conducted by people of many disciplines none of whom has lifted a scalpel or looked through a microscope or interpreted laboratory data or even more to the point, made a critical medical decision and then waited out the long anxious process that constitutes recovery. The insights of the physician are absent from these planning committees, the physician's input minimized and at times even neglected.

Long years of study change a man. So do thirty years of sleeping with a telephone beside his bed or analyzing the data or making a difficult diagnosis or sweating out the healing process. The man who has walked that road has much to contribute of his knowledge and insight, but unfortunately these contributions seem to be relegated to obscurity. The health planners present pristine concepts devoid of input from what many of them considered a special interest group. The plans are sterile for this absence. If put into effect they will serve the people of America poorly. It could be different. It isn't. More is the pity!

John J Regan

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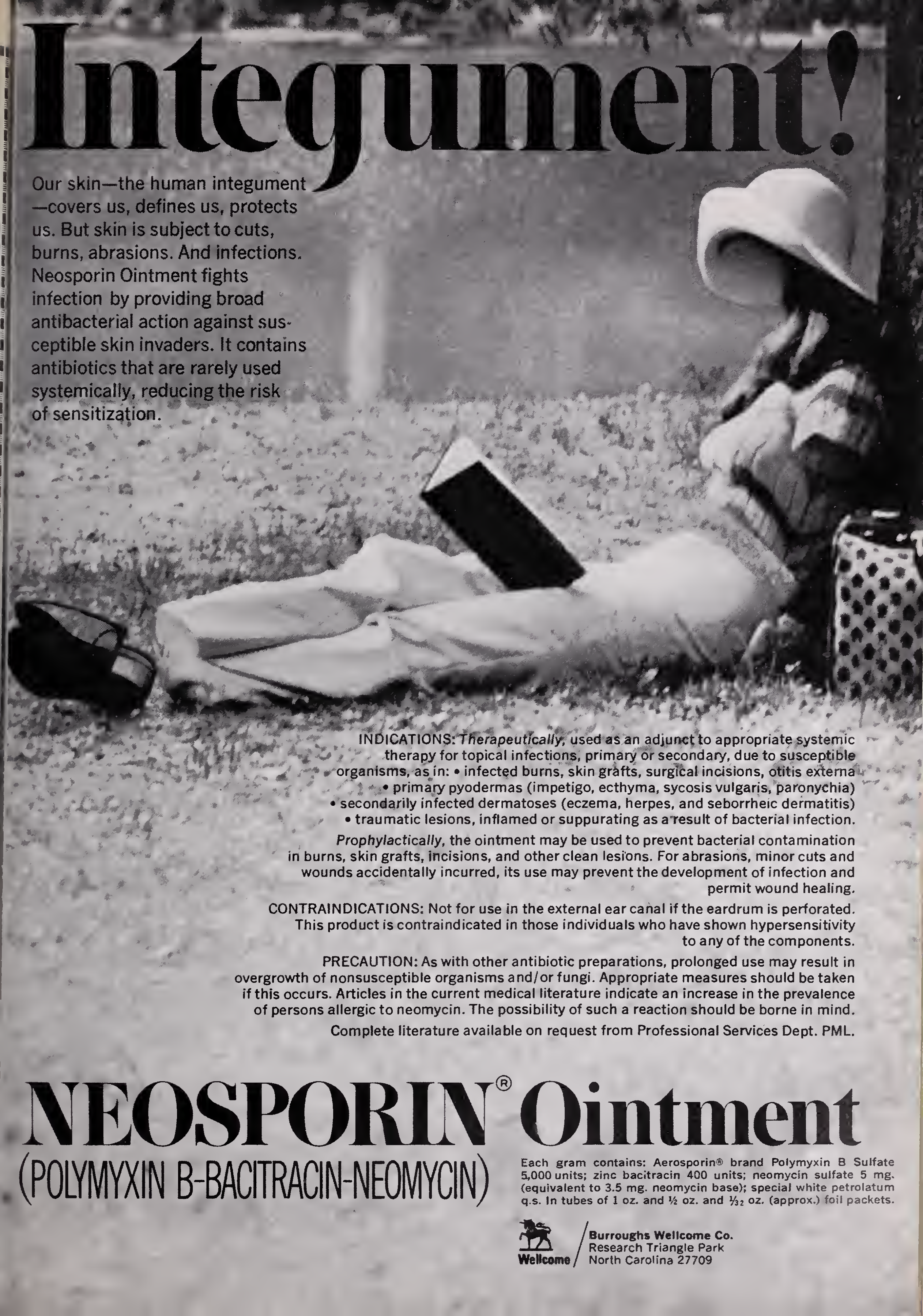

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Contraindications: Known hypersensitivity to flurazepam HCl

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e g , operating machinery, driving) Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards Not recommended for use in persons under 15 years of age Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation dizziness and/or ataxia If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects Employ usual precautions in patients who are severely depressed or with latent depression or suicidal tendencies Periodic blood counts and liver and kidney function tests are advised during repeated therapy Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering ataxia and falling have occurred, particularly in elderly or debilitated patients Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints There have also been rare occurrences of sweating, flushes, difficulty in focusing blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase Paradoxical reactions, *e g* , excitement, stimulation and hyperactivity, have also been reported in rare instances

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of patients. Productive coopera-
ıas been achieved through
ıal respect as well as a common
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ce. This mutual respect has been
cted, in part, by joint support
the years for the adoption and
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ifically prohibiting unauthorized
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ɔasic principles of medical, den-
ıd pharmacy practice are thus
ed and preserved in the interest
tient welfare.

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essional status of pharmacy any
than they have in and of them-
s guaranteed absolute protec-
from unsafe drugs, or freed
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rged to increase the frequency
regularity of their contacts with
macists in selection of quality
products, recognizing that economies to patients can be improved through such communication, taking into account the patients' needs. The pharmacist's knowledge of the chemical characteristics of drugs, their mode of action, toxic properties and other characteristics that assist in making drug selection decisions should be utilized to the fullest extent practicable by physicians and dentists in serving their patients.

Since drug product selection entails knowledge derived from clinical experience, the physician's and dentist's roles in product selection remain primary and do not permit delegation of decisions requiring medical and dental judgments. A broader role in therapy will evolve for pharmacists as improved understanding and cooperation among the professions continue to grow.

There has been no evidence that there are convincing reasons to modify or repeal existing laws and regulations prohibiting the unauthorized substitution of another drug product for the one specified by a prescriber. It is our belief that such laws and regulations merit the joint support of the medical, dental and pharmaceutical professions and the pharmaceutical industry.

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Urinary Tract Trauma

ALEXANDER S. CASS, M.D.* and GERALD W. IRELAND, M.D.*

Immediate radiological evaluation of the injured urinary tract is necessary if immediate surgical management of the more severe degrees of injury is to result in primary repair of the damaged urinary tract. This radiological evaluation consists of an infusion or large dose intravenous pyelogram. In patients with associated abdominal visceral injury the excretory urogram should be carried out at the same time as the laparotomy. A cystogram with up to 400 mls. of dye and a post washout film is necessary to exclude rupture of the bladder. A retrograde urethrogram is indicated when there is blood at the external meatus or inability to pass a soft urethral catheter into the bladder.

EXCISION OF DEVITALIZED tissue following trauma with primary repair has given superior results to healing by secondary intention. It is felt that a similar approach to urinary tract trauma would result in reduced morbidity and hospitalization and greater preservation of function. Immediate radiological evaluation with an accurate diagnosis is mandatory with this approach of immediate surgical management of urinary tract trauma.

Protocol

Urine obtained by immediate voiding or urethral catheterization is examined for hematuria (Chart). If blood is present at the external urinary meatus or there is inability to pass a soft #18 French Foley's catheter via the urethra into the bladder, a retrograde urethrogram is performed to evaluate the integrity of the urethra. The retrograde urethrogram is performed with 10 cc. of Renografin 30% injected into the urethra with a syringe and Brodny clamp.

If macroscopic or microscopic hematuria is present, a retrograde cystogram is performed via a urethral catheter by instilling 250 mls. of Renografin 30% into the bladder. If no extravasation is seen by anteroposterior roentgenogram a further 150 mls. is instilled and another roentgenogram taken. The bladder is then emptied and washed out with normal saline before a post washout film is taken to detect extraperitoneal extravasation anterior or posterior to the bladder and not seen on roentgenograms with the bladder full of dye.

CHART

Management

A. Severe trauma

Catheterize on O.R. table ↓ **Hematuria Cystogram + IVP on O.R. table** ↓

Perirenal hematoma found at laparotomy ↓ **IVP on O.R. table** ↓

Positive X-Ray findings
Exploration

B. Less severe trauma

Hematuria, pain, tenderness, mass.

↓

Cystogram & IVP ± arteriogram

↓

Positive X-Ray findings
Exploration

C. Both groups

Blood at external urinary meatus or inability to pass soft catheter via urethra

↓

Retrograde urethrogram then cystogram & IVP ± arteriogram

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Presented at the 120th Annual Meeting of the Minnesota State Medical Association, May, 1973, Minneapolis, Minnesota.
See editorial, page 45.

An excretory urogram is then performed with a large dose of dye or an infusion IVP. Renografin 60%, adult 1 cc/Kg, or child—20-40 cc. is used. With an infusion urogram, 1 cc. of Renografin 60% per pound of body weight added to 5% Dextrose in water to make a 300 ml. infusion is used.

During a laparotomy for visceral injury the presence of a perirenal or retroperitoneal hematoma indicates that a urogram be carried out while the laparotomy is in progress. A specially modified operating room table with a radiographic table top including a Bucky unit allows for diagnostic quality urogram to be carried out during the surgical procedure (Figure 1).

In a less severely injured patient who has hematuria, a cystogram followed by a washout film and excretory urogram are also performed. The presence of pain in the side of the abdomen or back, tenderness with muscle guarding or a mass in the abdomen or flank, without the presence of hematuria, makes an excretory urogram mandatory.

Injuries to the Kidney

If an excretory or infusion urogram reveals non-function, distortion of calyces or extravasation, further evaluation is indicated. A renal arteriogram is preferable to a cystoscopy and retrograde pyelogram, as the failure to excrete dye is due to a lesion of the renal parenchyma or to its blood supply rather than to a lesion of the drainage system which is outlined by retrograde pyelogram. A normal calyceal pattern on retrograde pyelogram does not exclude a severe pathological lesion of the kidney such as infarct or ruptured renal pedicle. The presence of a definite large devascularized segment on arteriography is an indication for exploration of the kidney. The positive urogram finding of nonfunction, distortion of calyces or extravasation found during a laparotomy is an indication for exploration of that kidney after clamping the renal vessels near the aorta. (Figure 2).

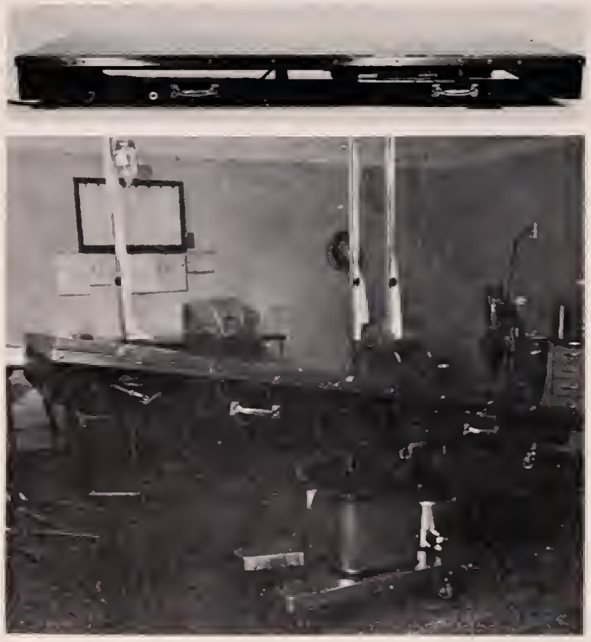

Fig. 1—(Top) Radiographic table top with movable Bucky system. (Bottom) Radiographic table top secured to a regular operating room table (Cass, A. S. et al.: Modification of An Operating Room Table for Immediate Radiographic Evaluation of the Urinary Tract in the Acute Severe Trauma Patient. J Urology 105:569, 1971).

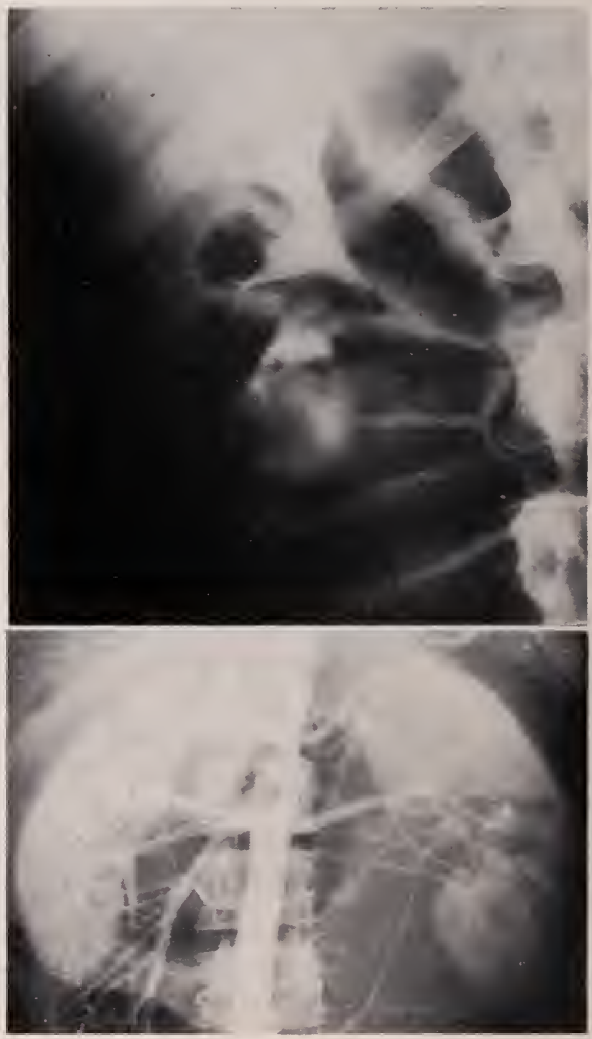

Fig. 2. (Top) IVP showing extravasation, lower pole right kidney (Reproduced J. Urol . (Bottom) Abdominal aortogram demonstrating lateral displacement of left kidney with avascular segment and some extravasation in mid kidney region.

Renal contusion is managed conservatively. The more severe degrees of renal injury comprising laceration, rupture and renal pedicle injury are managed surgically.

Injuries to the Ureter

The diagnosis of ureteral injury may be made early at the time of immediate laparotomy for associated injury to abdominal viscera or it may be delayed and present as a urinary fistula, a retroperitoneal infected mass or an extravasation seen on excretory urogram. A retrograde pyelogram confirms the diagnosis with extravasation of dye from the ureteral disruption.

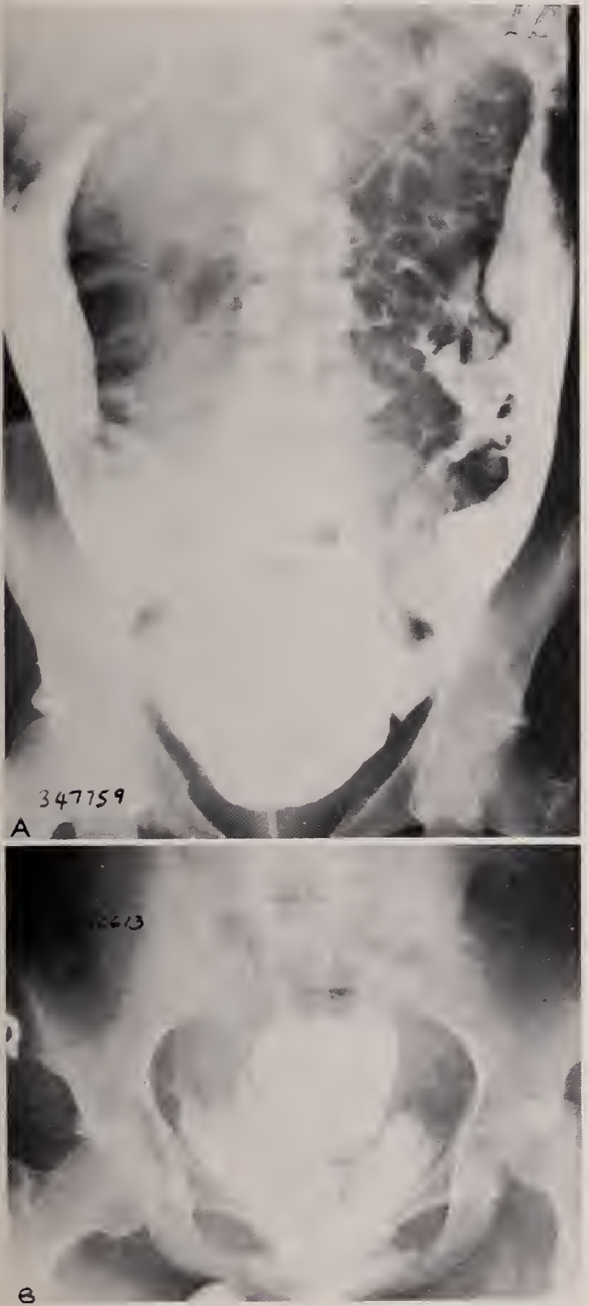

Fig. 3—(A-top) Cystogram showing intraperitoneal rupture of the bladder. (B-bottom) Cystogram showing extraperitoneal rupture of the bladder. (Cass, A. S. and Ireland, G. W.: Bladder Trauma Associated with Pelvic Failures in Severely Injured Patients. J Trauma 13:3:205, 1973).

If the diagnosis of ureteral injury is made early at the time of laparotomy for associated abdominal visceral injury, the treatment is primary surgical repair. With delayed presentation of ureteral injury, nephrostomy or nephrectomy with drainage of the mass or extravasation is performed, depending upon the patient's general condition and status of the contralateral kidney.

Injuries to the Urinary Bladder

With contusion of the bladder no extravasation of dye is seen on cystogram. However, there may be displacement of the bladder resulting from a large extraperitoneal hematoma accompanying a pelvic fracture.

Intraperitoneal extravasation outlining loops of bowel and the paracolic gutters is seen with a cystogram performed with intraperitoneal rupture of the bladder. Extraperitoneal extravasation of dye is seen especially on the post washout film with extraperitoneal rupture of the bladder due to blunt trauma which also results in a fractured pelvis (Figure 3).

The treatment of bladder contusion is conservative while the treatment of ruptured bladder is surgical with repair of the rupture, if large, suprapubic cystostomy, prevesical drain and urethral catheter.

Injuries to the Urethra

Complete rupture of the urethra is diagnosed by retrograde urethrogram when there is gross extravasation at the site of urethral injury with no dye passing into the proximal urethra or

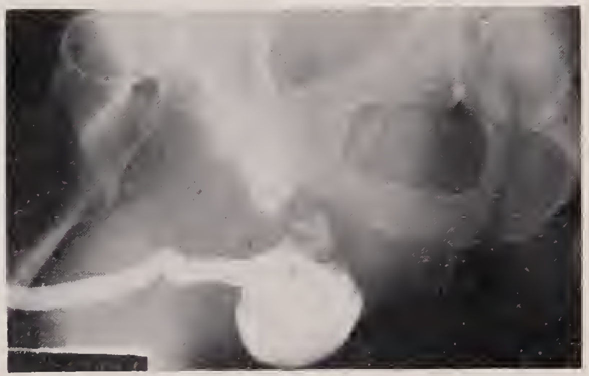

Fig. 4—Retrograde urethrogram demonstrating complete rupture of the bulbous urethra.

bladder. There is also inability to pass a soft urethral catheter. Partial rupture of the urethra is diagnosed by a localized extravasation on retrograde urethrogram and some dye passing into the proximal urethra and bladder. A soft urethral catheter is also able to be passed into the bladder (Figure 4).

Treatment of partial rupture of the urethra is suprapubic cystostomy or a urethral catheter. Complete rupture of the urethra is managed by suprapubic cystostomy, realignment of the urethra followed by primary repair or urethral catheter stinting and drainage of the area.

MEDICINE IN CRISIS

CRISIS IN MEDICINE

Minnesota State Medical Association
121st Annual Meeting
Duluth, Minnesota
May 16-17, 1974

"Crisis" is a word with which we are becoming very familiar. Fuel crisis, energy crisis, and we've heard rumblings of a food crisis; the future is clouded with crises we will overcome with much deliberation and planning.

So is the future of medicine clouded by crises; and so will they be overcome with much deliberation and planning.

Although physicians live in a world of daily crises—medical, surgical, obstetrical, pediatric, etc., the new crises that are appearing on the horizon—energy, social, economic, political—involve medicine. Because these are frequently interlaced with medical crises, it is timely to discuss the effect of this on the quality of medical practice, family involvement, community impact, physician-patient relationships, physician-hospital relationships, and many other topics that have bearing on the practice of our profession.

In this age of rapid progress in technology and research, the physician is faced with another crisis—that of keeping abreast of the advances in methods of treatment, the increase in understanding of heretofore unknown or little understood functions of body systems, the remarkable discoveries, and newfound applications of answers to a variety of problems. We have the need as well to take a closer look at the social, economic, and political problems facing the medical profession. And that's what the scientific program for the annual meeting is all about.

The Scientific Assembly Committee has chosen as the theme of the Scientific Session of the annual Minnesota State Medical Association meeting "MEDICINE IN CRISIS/CRISIS IN MEDICINE." It is our objective to present both crisis situations to our membership, and to show that both are frequently and intimately intertwined.

The Scientific Session of the 121st Annual Meeting will be an accredited Continuing Medical Education Program under the auspices of the American Medical Association. We know that our concerns about the problems facing the medical profession are shared by the membership, and we are endeavoring to structure a program that will be stimulating, educational, and informative to all.

Mark your calendar now to attend the most important scientific program of the year.

Robert D. Semsch, M.D.
Chairman, Scientific Assembly Committee

Late Toxic Effects of Cytotoxic Drugs

I. E. FORTUNY, M.D.* and A. THEOLOGIDES, M.D., Ph.D., F.A.C.P.

The usefulness of cytotoxic drugs has expanded from the malignant neoplastic diseases to a great variety of syndromes of known and unknown etiology and pathogenesis. For the management of these conditions a prolonged use of cytotoxic drugs is usually required; which will undoubtedly increase the late toxic effects and produce complications.

The spectrum of usefulness of cytotoxic drugs has been expanded from malignant neoplastic diseases to a great variety of inflammatory, autoimmune and other conditions of unknown etiology. Rheumatoid arthritis, systemic lupus erythematosus, iridocyclitis, nephritis, nephrosis, psoriasis, uveitis, ulcerative colitis, chronic active hepatitis, pyoderma grangrenosum, multiple sclerosis. Goodpasture's syndrome, pure red cell aplasia, idiopathic thrombocytopenia and sarcoidosis are among the conditions in which the effectiveness of these agents has been proven or is under evaluation.[1]

The acute toxicity of these drugs is well known, and as a rule, is the result of their effect on rapidly proliferating tissues of the body such as the bone marrow, the gastrointestinal mucosa and the hair follicles.

The control of both malignant and non-malignant diseases usually requires prolonged administration of such cytotoxic agents. Their prolonged use often produces chronic toxicity and results in complications that might be irreversible even when the drug is discontinued. An increasing number of late toxic effects and chronic complications are being recognized gradually, and the more important ones are reviewed in this article.

Neurologic Complications

A variety of neurologic complications can result from the use of cytotoxic agents, of which vincristine appears to have the wider spectrum of early and late toxic effects.[2] Among the more predictable abnormalities produced by vincristine are loss of deep tendon reflexes and paresthesias observed in up to 82% of patients,[2] and gradually followed by muscle weakness and atrophy. Late effects after prolonged use may result in oculomotor paresis up to 50% of patients,[3] paresis of other cranial nerves, loss of salivation, paralytic ileus and bladder atony.[2] Depression, anxiety and hallucinations are also seen. Seizures have been observed following the long term use of vincristine,[2] chlorambucil,[4] nitrogen mustard and 5-fluorouracil.[6] Personality disturbances and mania or depression have been described with the use of procarbazine[5] and L-asparaginase.[7]

Liver Toxicity

Hepatic fibrosis precedes abnormalities in liver function tests and, which if unsuspected, may lead to portal hypertension following prolonged administration of methotrexate.[8] Intrahepatic cholestasis and focal necrosis of Kupfer cells does occur after prolonged use of 6-mercaptopurine,[9] focal necrosis of liver has resulted after long term use of cyclophosphamide.[10]

Lung Toxicity

Functional and structural changes of the lung may develop following long term use of cytotoxic agents. The most frequent offender appeared to be busulfan, and the clinical picture of progressive shortness of breath, and diffuse interstitial infiltrates on chest roentgenogram have been demonstrated histologically to be the result of fibrinous edema with hyaline membrane formation leading to inter- and intra-alveolar fibrosis.[11] A decrease

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in pulmonary diffusing capacity and dose dependent interstitial pulmonary fibrosis may be expected in up to 80% of patients treated with bleomycin.[12] Alveolar dysplasia and hyaline membrane production has been described also with the prolonged administration of cyclophosphamide.[13,14]

A clinical picture characterized by a hypersensitivity reaction with fever, cough, dyspnea, cyanosis, eosinophilia, diffuse pulmonary infiltrates may develop acutely after long term use of methotrexate[15] or procarbazine.[16] In the former, lung biopsy demonstrated an allergic granulomatous pneumonitis with angiitis.[15]

Kidney and Urinary Tract Complications

Kidney toxicity after long term use of cytotoxic drugs may proceed from mild elevation of the blood urea nitrogen and decreased creatinine clearance to complete anuria due to significant glomerular and tubular damage.

Administration of methotrexate has resulted in tubular necrosis and uremia, but the actual incidence is not known.[18] Crystaluria and hematuria have occurred following the use of 6-mercaptopurine.[17] Hemorrhagic cystitis, pyelitis and urethritis from cyclophosphamide administration, may present either early or insidiously late.[20] The incidence of this complication can be as high as forty percent of patients receiving the drug.

Effects on the Skin and Its Appendages

Chronic skin changes may result from the use of cytotoxic drugs. These effects vary, ranging from facial flush with the use of mithramycin to dermal atrophy after hydroxyurea and vinblastine therapy.[19] Maculopapular rashes are observed with the use of nitrogen mustard, 5-fluorouracil and procarbazine.[9,17] Melanoderma has been encountered after prolonged use of thiotepa, methotrexate and busulfan.[21,22]

Alopecia is a well-known effect of cytotoxic drugs and its development may be rapid or gradual after prolonged therapy. Nail changes include dullness, brittleness, white linear streaking, periungal fungoid hypertrophy and rarely complete loss of nails.

Endocrine Gland Complications

Gonadal atrophy and sterility are well-documented results of prolonged administration of cyclophosphamide.[20,24] Testicular biopsies have shown that during the first four months of treatment, the predominant effect of this drug is oligospermia followed by testicular atrophy after eight to 10 months of continuous therapy at a dose of 50-100 mg per day.[25] Amenorrhea begins in 20% of women after six months of continuous therapy and in half the patients it is accompanied by menopausal symptoms, increase in gonadotropins and loss of stratification of the vaginal epithelium, when the drug is continued for more than eight months.[24] Permanent azoospermia follows the use of mithramycin.

Pseudoadrenal insufficiency following long term use of busulfan, and consisting of skin hyperpigmentation, weakness, fatigue, weight loss, anorexia, nausea and hypotension, but lacking mucous membrane pigmentation and hypoglycemia and with normal levels of 17-hydroxycorticosteroids and 17-ketosteroids but increased levels of melanophore stimulating hormone has been described.[22]

Gynecomastia, tender unilateral, sub-areolar hypertrophy of mammary tissue règressing spontaneously has been described following the use of vincristine[26] and busulfan.[27]

Congenital Malformation

Congenital anomalies following the use of methotrexate,[28,29] cyclophosphamide, chlorambucil and 6-mercaptopurine[28,30] have been described in women treated with these drugs before and during pregnancy.

If methotrexate is used in the first trimester of pregnancy, fetal abnormalities and/or abortion are almost inevitable results.[29] Cyclophosphamide has only occasionally been found to produce these abnormalities and in the only reported case, irradiation was also a co-factor.[31]

Hematologic Effects

Megaloblastic changes in the bone marrow are observed following the long term administration of hydroxyurea,[19] 5-fluorouracil,[32] and methotrexate.[21] Bone marrow aplasia is the most significant toxic effect following prolonged use of anticancer agents. Thrombocytopenia, especially, is the rule with maintenance or pulse therapies with these drugs with the exception of vincristine which might even produce thrombocytosis.[33] Hemolytic anemia may be encountered after long term use of procarbazine.[34]

Gastrointestinal Effects

The gastrointestinal mucosa is sensitive not only to short but also to long term cytotoxic therapy. The potential development of intestinal malabsorption following long term cytotoxic therapy may be considerable. With methotrexate administration, mitotic inhibition of duodenal and jejunal epithelium have been shown to be followed by structural damage to the crypt and villous epithelium.[35] Disturbances of intestinal motility impairing bowel function are observed with the long term use of cytotoxic drugs, and as already mentioned, vincristine may produce paralytic ileus.[2,9]

Eye and Ear Complications

The development of cataracts following busulfan therapy is associated with polychromatic lenticular changes and posterior subcapsular opacities.[36]

We have observed mild to moderate unilateral and bilateral loss of auditory acuity in patients receiving combination chemotherapy for leukemia and lymphoma, but these of course might represent complications of the disease rather than the treatment.

Cardiovascular Effects

Interruption of the adrenergic sympathetic system following long term use of vincristine and manifested by orthostatic hypotension, bradycardia and diaphoresis and absent norepinephrine excretion has been described.[37] Dose dependent myocardiopathy follows the use of Daunorubicine[50] or adriamycin.[51]

Bone Changes

The prolonged use of methotrexate in leukemia children has resulted in osteoporosis which in a few instances resulted in spontaneous fractures.[38]

Immunosuppression

Cytotoxic drugs have been found to suppress humoral and cellular immune responses. The primary humoral response of antibody production can be blocked by cyclophosphamide,[44] 6-mercaptopurine,[45] procarbazine[46] and cytosine arabinoside.[47] The secondary response, antigen handling, complex formation and differentiation can also be blocked by these agents; in decreasing order of potency, cyclophosphamide, methotrexate, 6-thioguanine, 6-mercaptopurine and to a lesser extent, 5-fluorouracil, have been shown to interfere with this type of humoral response.[20,44] Cellular immunity, judged by the patient's ability to produce a delayed hypersensitivity reaction to bacterial and fungal antigens, to mount a skin graft rejection or to respond to chemical sensitization, can be altered by cytotoxic agents[39,40,44-48] Nonspecific inflammatory response of granulocytes and mononuclear cells, by the use of the skin window, can be blocked by prolonged exposure to cytotoxic agents.[49]

Carcinogenic Effects

Immunosuppression following long term use of cytotoxic agents increases the prevalence of neoplastic transformation. As the survival of cancer patients successfully treated with cytotoxic drugs increases, the emergence of additional malignancies is being recognized.

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17-51. Will be found on page 55.

Macroglobulin-Producing Histiocytic Lymphoma

Of Hepatic Origin

JOHN B. CARTER, M.D.*

A histiocytic lymphoma restricted to the liver was associated with macroglobulinemia. IgM levels, as determined by radial immunodiffusion methods, were four to six times normal while levels of IgG and IgA were below the normal range. Immunoglobulin production by tumor cells was supported by the presence of PAS-positive nuclear and cytoplasmic inclusions.

THE ASSOCIATION of macroglobulinemia with malignant lymphomas has been recognized recently.[1,2] The association of immunoglobulin production with extranodal lymphosarcomas is less well recognized but has been documented in a few cases.[3-6]

The present report describes a case of a solitary histiocytic lymphoma of the left hepatic lobe associated with macroglobulinemia. Production of macroglobulin by tumor cells was demonstrated histochemically.

Report of Case

Clinical Features

The patient, an 84-year-old white woman, had been in good health until she was hospitalized with anemia and generalized weakness. Physical examination showed a questionable epigastric mass. There was no lymphadenopathy.

Hematologic studies revealed a hemoglobin concentration of 9.5 gm./100 ml. of blood, a normocytic blood picture, and reticulocyte counts of 1.5 to 2.0%. The value for serum iron was 52 mg./100 ml., and the total iron-binding capacity was 212 mg./100 ml. White blood count was 6,400 with a normal differential. Aspiration of bone marrow showed moderate erythroid hyperplasia (37.6%) with a normal percentage of mature lymphocytes (15.3%), and only rare plasma cells that were morphologically normal. Platelet counts were 120,000 to 140,000/mm.^{3} of blood, and coagulation parameters were normal. Sedimentation rates were 45 to 55 mm./hour.

The value for serum uric acid was 8.8 mg./100 ml. and for serum alkaline phosphatase 350 mU/ml. Liver function studies revealed a total protein level of 5.7 gm./100 ml., thymol turbidity of 14 units, a level of serum glutamic oxalacetic transaminase of 50 mU./ml. and normal levels of bilirubin. Bromsulphalein retention was 5% at 45 minutes. Qualitative tests for cryoglobulin and cryofibrinogen were positive; qualitative urinary tests for Bence-Jones proteins gave negative results. Serum electrophoresis disclosed a small gamma peak and a serum albumin level of 2.8 gm../100 ml. Quantitation of immunoglobulin by the agar-gel radial immunodiffusion method showed markedly increased serum levels of IgM with subnormal levels of the other immunoglobulins: IgG 0.40 gm./100 ml.; IgA, 0.52 gm./100 ml.; and IgM, 1.16 gm./100 ml. One week later, the IgM level was 0.72 gm./100 ml. and the levels of IgG and IgA remained below normal.

Bone Xrays showed severe Paget's disease of the skull, sacrum and humerus. This was apparently responsible for the high serum levels of alkaline phosphatase. A gastrointestinal series, abdominal lymphangiogram and x-ray studies of the vertebral bodies showed no abnormalities. A liver scan was interpreted as showing decreased pliability and a non-uniform uptake pattern. Needle biopsy of the liver contained a malignant lymphoid infiltrate interpreted as a malignant lymphoma.

The clinical impression, based on these findings, was that the patient had a form of Waldenstrom's macroglobulinemia. Chlorambucil therapy was instituted but was ineffective. Readmission to the hospital was necessary four months later for a short time due to progressive anemia and fatigue. An enlarging epigastric mass was noted subsequent to this hospitalization. The patient expired at home six months after her initial hospitalization.

Pathologic Features

Significant at autopsy were the unexpected absence of systemic disease and the presence of a large hepatic

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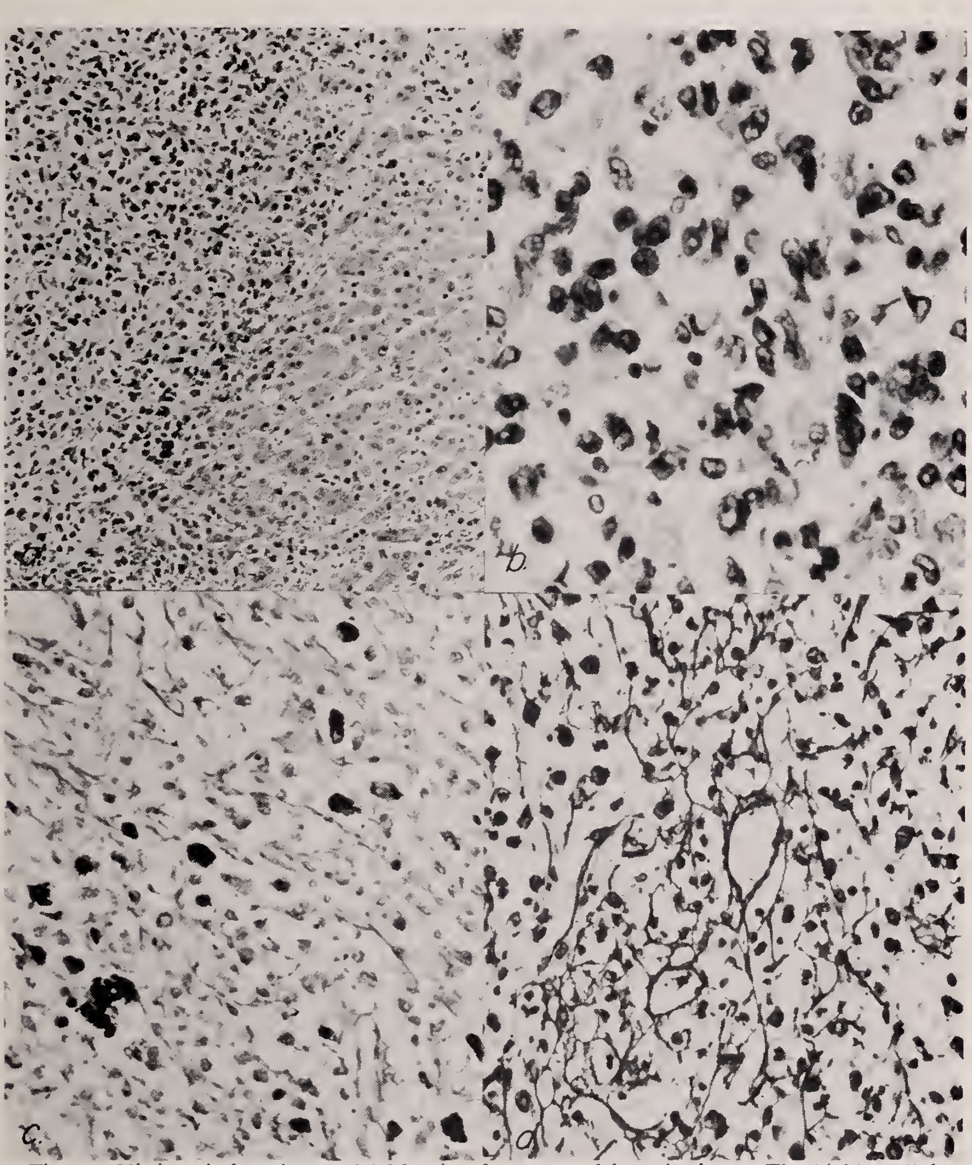
tumor. Cachexia was prominent. The liver weighed 3,200 gm. A soft, gray, fleshy tumor, 18 cm. in diameter, replaced and enlarged most of the left lobe of the liver. Dissemination was limited to several satellite nodules 1.0 to 2.5 cm. in diameter. The tumor did not extend beyond the hepatic substance, and there was neither regional nor systemic lymphadenopathy. The biliary tract was not involved.

Histologically, the tumor consisted of densely cellular sheets of highly pleomorphic lymphoreticular cells. These cells were distinct from surrounding hepatocytes and did not resemble a hepatocellular tumor (Figure 1*a*). Nuclear pleomorphism was prominent and many cells contained two or three nuclei, some with prominent nucleoli (Figure 1*b*). None met the morphologic criteria for Reed-Sternberg cells. The tumor was classified as a histiocytic lymphoma,[7] primary in the liver.

Evidence supporting the production of macroglobulin by the tumor cells was the conspicuously positive staining of the tumor sections by periodic acid Schiff (PAS), as described by Dutcher and Fahey[8] and Brittin et al.[9] This stain showed numerous intranuclear inclusions (Dutcher bodies) and cytoplasmic inclusions (Mott cells and Russell bodies). Histologic study of the bone marrow and spleen showed no abnormal cellularity in sections stained with either hematoxylin and eosin or PAS.



Figure—Histiocytic lymphoma. *(a)* Margin of tumor and hepatic tissue. The highly cellular, pleomorphic appearance was consistent throughout the tumor. H & E, x 120. *(b)* High power view of tumor cells. Marked nuclear pleomorphism and numerous multinucleated cells are evident. A large cytoplasmic inclusion can be seen in the cell in the center of the field. H & E, x 450. *(c)* Numerous tumor cells containing cytoplasmic and nuclear material that is heavily PAS positive. Higher power examination showed many inclusions that were specifically intranuclear. PAS, x 240. *(d)* Reticulum pattern of the tumor is heavy but the individual tumor cells are not completely enveloped by reticulin fibers. Gomori-reticulum stain, x 240.

Comment

The tumor in this case is essentially a lymphoreticular tumor, originating in the liver, classified as a histiocytic lymphoma. The tumor cells were capable of producing macroglobulin as demonstrated by intracellular glycoprotein accumulation. Quantitation of serum immunoglobulins showed a four to six-fold increase in IgM levels. IgG and IgA levels were below normal on two occasions. Increase of only one class of immunoglobin (IgM) supports the impression of primary macroglobulinemia rather than a secondary or reactive increase in immunoglobulins in all forms elevated. Production of glycoprotein by individual tumor cells was documented by histochemical means (PAS stains).[8-10] While immunofluorescent studies, unfortunately, were not available, the presence of PAS-positive intranuclear inclusions has been described as evidence of cellular elaboration of glycoprotein,[8,9] and has been subsequently accepted by other authors[2] as evidence of immunoglobulin production by specific cells.

The association of monoclonal gammopathy with solitary lymphoreticular tumors has been reported with increasing frequency in recent years,[11,12] probably as a result of the increased technical feasibility of determining serum levels of immunoglobulins. Moore and associates,[1] studying a large series of cases of malignant lymphomas, found that a significant number of such tumors are capable of producing immunoglobulin (IgM). These investigators also determined that the relationship of increased IgG levels to malignant lymphoma was coincidental. None of their cases showed increased levels of IgA.

The association of macroglobulinemia with solitary tumors appears to be much less common. Migliore and associates studied a large series of cases involving neoplastic diseases and determined that the coexistence of monoclonal gammopathy and nonlymphatic malignant lesions was coincidental.[13]

Prasad and Bloch[5] reported a case of lymphosarcoma of the brain associated with increased IgM levels. IgM levels returned to normal after the surgical removal of the tumor. Autopsy findings were not available and histochemical findings were not reported but the case history suggests that the lymphomatous process was disseminated.

In the case presented by Alami and associates,[3] an extranodal lymphosarcoma involving the liver was associated with macroglobulinemia and increased levels of IgG. IgA levels were in the low-normal range. The lymphomatous process appeared to involve the marrow also, as lymphocytosis was marked in the marrow. Histochemical studies did not suggest the production of glycoprotein by tumor cells or by marrow lymphocytes.

The present case illustrates the point that macroglobulinemia may be due to a solitary lymphoma as well as the more usual situation of diffuse neoplastic involvement of the reticulo-endothelial system. The overlapping characteristics of classes of lymphoid malignancies is also apparent. If the immune system is viewed as a dual component system with thymic dependent (T cell) and thymic independent (B cell) components,[14] the tumor in the present case can be viewed as a malignant proliferation of a clone of thymic independent cells (B cells). These cells are capable of producing humoral antibodies or circulating immunoglobulin, of which IgM is one type.

Although the specific name of histiocytic lymphoma was given to the tumor in our case, such precise categorization of the tumor by light microscopic criteria may not serve as much purpose as the recognition of its function. Specifically, the latter indicates that the malignant cell population is sufficiently well differentiated to retain its functional capacity of producing macroglobulins. Functional criteria, indeed, may provide a useful framework for classification of lymphoid tumors as the specific functions of the several components of the immune system are clarified.

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9-14. Will be found on page 30.

Bacteriuria in Spinal Cord Lesion Patients

With Ileac Diversions

ELLEN NEWMAN, M.S., M.T.* and MARY PRICE, M.D.†

Urinary tract infections in patients with ileac diversions are a complex problem because of the frequency of bacteriuria in these patients, and one which needs continued study.[1,5,8]

SPINAL CORD LESION-PATIENTS having ileac diversions for urinary drainage exhibit a high incidence of bacteriuria.[1-5] There is a need for a better understanding of the presence of bacteria in urine of these patients.

This study was conducted to help answer several questions. What is true bacteriuria and what is contamination? Is the incidence of positive cultures due to continuing infection or new infections? What are the sources of these infections?

Results indicate that microflora on the stoma present a possible source of contamination when obtaining specimens for urine culture and a source of infection for the patient if proper care is not taken with urine collecting appliances. The telescopic double lumen catheter provides a suitable

TABLE 1

Patient	Stoma Swab Cultures	Loop Cultures*
A	Pseudomonas, Streptococcus	Sterile
B	Proteus mirabilis, Pseudomonas, Escherichia coli, Alpha streptococcus enterococcus	Proteus mirabilis, Citrobacter freundii
C	Klebsiella	Klebsiella, Escherichia coli
D	Providence, Proteus mirabilis, Alpha streptococcus enterococcus, Escherichia coli, Enterobacter	Enterobacter
E	Escherichia coli, Providence, Pseudomonas aeruginosa	Sterile
F	Proteus morgani, Pseudomonas, Proteus rettgeri, Alpha streptococcus enterococcus, Alpha streptococcus non-enterococcus	Proteus morgani, Proteus rettgeri, Pseudomonas aeruginosa
G	Pseudomonas aeruginosa	Pseudomonas aeruginosa
H	Candida albicans	Sterile
I	Proteus mirabilis, Klebsiella, Pseudomonas aeruginosa, Alpha streptococcus enterococcus, Proteus rettgeri, Alcaligenes	Pseudomonas aeruginosa, Alpha streptococcus enterococcus, Proteus morgani
J	Proteus mirabilis, Alpha streptococcus, Pseudomonas aeruginosa, Proteus morgani, Escherichia coli, Serratia marcesens	Escherichia coli

*Specimens obtained using telescopic double lumen catheter procedure.

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method of obtaining specimens for culture. Sequential post-operative cultures from five patients are presented to demonstrate the need for follow-up cultures in determining what concentration of micro-organisms should be considered significant and treated, and the difficulty of eradicating bacteriuria in these patients.

Methodology

Forty-eight cultures were made of urine specimens from 26 spinal cord lesion-patients with ileac diversions. Specimens were obtained using double lumen catheterization as described by Spence, et al.[6] A telescopic double lumen catheter was passed into the ileal conduit through a carefully cleansed stoma using sterile technique. Specimens were taken directly to the University Hospital Microbiology Laboratory for culturing, or refrigerated for delivery within the hour.

Prior to aspirating the urine samples, qualitative cultures were made of bacterial flora in the stoma area, after the collective appliance had been removed with sterile gauze or cotton. A sterile swab was then gently wiped over the mucous membrane around the stoma opening. The swabs were placed in culture tubes and sent to the Microbiology Laboratory along with the urine cultures. The stoma area was then cleansed for catheterization.

All urine cultures were followed by disc diffusion tests for antibiotic sensitivity. Antibiotic treatment was based upon the results of the sensitivity tests.

Results

Forty-eight urine cultures were obtained from 26 spinal cord-injured patients with ileac diversions by means of a double lumen catheter technique.

Eleven cultures, or 22.9%, showed no growth. Four cultures, 8.3%, showed growth of less than 1,000 col/ml. Eighteen cultures, 37.5%, showed growth of organisms in concentrations between 1,000 and 100,000 col/ml. In 15 cultures, 31.3%,

TABLE 2

Date	Ileal Loop Urine Culture Colonies/Ml.		Stoma Swab Culture	Treatment
Mar. 1972	100,000+ 8,000	Proteus mirabilis Citrobacter freundii	Proteus mirabilis, Pseudomonas sp. Escherichia coli Alpha Streptococcus enterococcus	Macrodantin
Sept. 1972	3,000 6,000	Proteus mirabilis Proteus morgani	Proteus morgani, Klebsiella Escherichia coli, Pseudomonas sp. Alpha Streptococcus	
Oct. 1972	3,000 10,000 9,000	Pseudomonas aerugenosis #1 Pseudomonas aerugenosis #2 Pseudomonas aerugenosis #3	Pseudomonas aerugenosis Proteus mirabilis,Klebsiella Escherichia coli Alpha Streptococcus enterococcus #1, #2	
Jan. 1973	100,000+ 30,000	Proteus mirabilis Pseudomonas aerugenosis	Proteus mirabilis Pseudomonas aerugenosis Escherichia coli Alpha Streptococcus enterococcus #1, #2	Macrodantin
Jan. 1973 (10 days later)	30,000 20,000 40	Pseudomonas aerugenosis #1 Pseudomonas aerugenosis #2 Pseudomonas aerugenosis #3	Pseudomonas sp. Corynebacterium	
Jan. 1973 (2 weeks later)	20,000	Pseudomonas aerugenosis	Pseudomonas aerugenosis Corynebacterium	Coly-Mycin*
Jan. 1973 (1 day later)	100,000+ 6,000	Pseudomonas aerugenosis #1 Pseudomonas aerugenosis #2		Coly-Mycin
Mar. 1973	30,000	Escherichia coli	Escherichia coli, Klebsiella Alpha Streptococcus enterococcus Proteus mirabilis, Proteus morgani Pseudomonas aerugenosis	Mandelamine Ascorbic acid Gantanol
Apr. 1973	2,000	Pseudomonas aerugenosis	Pseudomonas aerugenosis Proteus morgani Citrobacter diversus	Tetracycline
May 1973	100,000+	Proteus mirabilis	Proteus sp. Gamma Streptococcus	Sulfisoxazole

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*By error started before culture taken withheld for 24 hours and recultured.

organism were found in greater than 100,000 col/ml. Twenty-two cultures contained more than one organism.

Table 1 shows a comparison of types of organisms found in urine cultures and stoma cultures of ten patients with ileac diversions, and indicates that by using careful sterile technique with a double lumen catheter it is possible to obtain sterile urine cultures even when large numbers of organisms are present on the stoma area. Micro-organisms present in the urine specimens obtained in this manner should be considered significant even when present in small concentration and follow-up cultures taken because they represent micro-organisms actually present in the urine as it collects in the ileal loop.

Follow-up cultures were taken from several patients. Results for five patients, evaluated in detail and recorded in Tables 2-6, demonstrate the difficulties of pharmacological management. Table 2 presents cultures from a C 5-6 quadriplegic man who had numerous urinary tract infections before and after the ileac diversion which was performed following a scrotal abscess and an intractible urethral cutaneous fistula.

Ten cultures were recorded over a period of 14 months. Because the young man had been inconsistent in taking prescribed antibiotics at home, he was admitted to the hospital for a supervised effort at sterilization of the urine. However, he left against medical advice (February) before the bacteriuria was eradicated.

The organism occurring most frequently was Pseudomonas aeruginosa, varying from 40 col/ml to greater than 100,000 col/ml. Proteus mirabilis had been present on several occasions in concentrations ranging from 3,000 col/ml to greater than 100,000 col/ml and was the organism present at the time of his last culture. Studies are being continued.

Table 3 represents a C 6-7 quadriplegic young man who received an ileac diversion in May 1971 because of repeated urinary tract infections and the development of right ureteral reflux. He was first referred to this laboratory in November 1972 at which time the urine culture was positive for Klebsiella sensitive to Gantanol. In one month, the Klebsiella appeared to be eradicated but Citrobacter, susceptible to Macrodantin was isolated from his urine. Gantanol was continued, 1 tablet daily, and Macrodantin was added to his regimen. Urine cultures one month later showed no growth and he was continued on Macrodantin and Gantanol. In March his urine culture still showed no growth and medication was changed to Mandelamine and Ascorbic acid.

Although sterile urine cultures were obtained twice, swab cultures continued to show bacterial growth on the stoma. Follow-up studies are being continued.

Table 4 represents a C5, complete, quadriplegic young man who had an ileac diversion January 1972. Before the diversion he had repeated urinary tract infections with multiple organisms and developed incomplete bilateral reflux. A urine culture immediately prior to surgery indicated the presence of Escherichia coli, Klebsiella, Proteus morgani, Proteus mirabilis, Alpha streptococcus enterococcus and Pseudomonas aeruginosa.

The tabulation of the follow-up cultures and the treatment of this patient demonstrates some of the difficulties and frustrations encountered while attempting to sterilize the urine. The follow-up cultures were taken during the year. At no time after the first post diversion culture was his

TABLE 3

Date	Ileal Loop Urine Culture Colonies/Ml.		Stoma Swab Culture	Treatment
Nov. 1972	100,000+	Klebsiella	Klebsiella, Proteus vulgaris Pseudomonas aerugenosis Alpha Streptococcus	Gantanol
Dec. 1972	50,000	Citrobacter diversus	Citrobacter diversus Alpha Streptococcus enterococcus Pseudomonas aerugenosis Escherichia coli	Gantanol Macrodantin
Jan. 1973	No Growth		Pseudomonas aerugenosis Escherichia coli Gamma Streptococcus	Gantanol Macrodantin
Mar. 1973	No Growth		Citrobacter diversus Pseudomonas aerugenosis Alpha Streptococcus	Mandelamine Ascorbic acid

urine free from bacteria, despite treatment with accepted dosages of drugs indicated by the antibiotic sensitivity studies. There was inexplicable fluctuation in the concentrations of bacteria. At times an organism would disappear from culture, only to return later. It is not known whether the patient was reinfected or if there was suppression of growth without complete eradication.

Table 5 represents a young C 4-5 quadriplegic with ileac diversion in June of 1969, following repeated urinary tract infections.

After his diversion, Pseudomonas continued to grow in concentrations varying from greater than 100,000 col/ml to 1,000 col/ml despite vigorous treatment. Bilateral renal calculi developed and the urologist discontinued all medications except Mandelamine and Ascorbic acid.

Table 6 represents a C5 quadriplegic young man who received an ileac diversion in February 1969 after numerous urinary tract infections. He has continued to have positive cultures since that time. The first culture in the series showed the presence of Enterobacter which was successfully treated with Macrodantin only to be replaced by Pseudomonas, and later by Citrobacter which persisted in spite of seemingly appropriate treatment. In April he developed nausea and diarrhea and it was necessary to discontinue all antibiotics. Follow-up will continue.

Discussion

We have found that the use of a telescopic double lumen catheter is a reliable method for obtaining uncontaminated specimens for urine cultures from patients with ileac diversions. Results in Table 1 indicate that it is possible to obtain specimens by this method without contamination from organisms present in the stoma area.

The demonstration of large numbers of potential pathogens on the stoma reinforces Creevy's[7] statement that the external stoma invites the entrance of bacteria. Kafetsioulis and his co-workers[8] pointed out that the lack of care of the ileostomy and poor hygienic management of the collecting appliance could lead to infections with urea splitting organisms. Appliances which do not drain freely permit stagnation of urine and replication of bacteria often indicated by an ammonical odor. Inadequate or infrequent cleansing of the collecting apparatus results in similar bacterial growth. Overfilling of the bag encourages reflux of grossly

TABLE 4

Date	Ileal Loop Urine Culture Colonies/Ml.		Stoma Swab Culture	Treatment
Mar. 1972	No Growth			
Apr. 1972	100,000+ 100	Proteus mirabilis Klebsiella		Macrodantin Gantanol
June 1972	7,000	Alpha Streptococcus enterococcus		Ampicillin
July 1972	100,000+ 15,000 50,000	Alpha Streptococcus enterococcus Pseudomonas aerugenosis Proteus morgani	Alpha Streptococcus enterococcus Pseudomonas aerugenosis Proteus mirabilis, Proteus rettgeri Klebsiella, Alcaligenes	Ampicillin
Sept. 1972	100,000+	Klebsiella	Klebsiella, Pseudomonas aerugenosis Proteus morgani, Proteus mirabilis Corynebacterium, Alpha Streptococcus enterococcus, Alcaligenes	Ampicillin Gantanol
Oct. 1972	100,000+ 8,000	Pseudomonas aerugenosis Proteus morgani	Pseudomonas aerugenosis Proteus morgani Klebsiella	Garamycin
Nov. 1972	50,000	Pseudomonas aerugenosis	Pseudomonas aerugenosis #1, #2 Candida albicans	Garamycin
Dec. 1972	6,000	Pseudomonas aerugenosis	Pseudomonas aerugenosis	Gantanol
Feb. 1973	7,000 600	Pseudomonas aerugenosis Proteus morgani	Pseudomonas aerugenosis, Proteus mirabilis, Corynebacterium Alpha Streptococcus enterococcus	Gantanol
Mar. 1973	20,000 20,000	Proteus mirabilis Proteus morgani	Proteus mirabilis, Corynebacterium Pseudomonas sp., Alpha Streptococcus enterococcus, Alpha Streptococcus non-enterococcus	Ampicillin

contaminated urine through the stoma into the ileal loop and up the ureters.

Tables 2 through 6 reveal some of the problems encountered in treating urinary tract infections. However the effect of such factors as the failure of patients to take medications as directed or the administration of other antibiotics by other physicians who are treating other infections cannot be tabulated.

The dependence of paralyzed patients upon family or attendants for daily care and often for administration of medications introduces another influence which does not lend itself to statistical analysis.

When evaluating results of urine cultures from patients with ileac diversions, it is necessary to keep in mind those factors which can influence the concentrations of organisms. Hinman[9] in 1968 reported that bacterial concentrations in urine from patients with ileac diversions will be reduced or washed out if the resident volume of urine is completely replaced before the bacteria present double in number. He noted that factors which interfere with calyceal, ureteral, or ileal motility perpetuate infection by lowering the rate of effective urinary replacement. The concentration of organisms present in urine cultures will be affected by the state of hydration, by the medication he has been receiving, by the peristaltic activity of the conduit and the state of the stoma.[9,10] It there-

TABLE 5

Date	Ileal Loop Urine Culture Colonies/M1.		Stoma Swab Culture	Treatment
Nov. 1972	100,000+	Pseudomonas aerugenosis	Pseudomonas aerugenosis #1, #2	Macrodantin Carbenicillin
Nov. 1972 (2 weeks later)	30,000	Pseudomonas aerugenosis	Providence	Carbenicillin
	15,000	Pseudomonas dimentis	Pseudomonas dimentis	Gantanol
	6,000	Providence		
Dec. 1972	100,000	Proteus rettgeri	Proteus rettgeri	Gantanol
	10,000	Pseudomonas sp.	Alcaligenes sp.	
Jan. 1973	20,000	Pseudomonas aerugenosis #1	Pseudomonas aerugenosis	Geocillin
	10,000	Pseudomonas aerugenosis #2	Pseudomonas sp.	Gantanol
	2,000	Pseudomonas aerugenosis #3		
Feb. 1973	100,000	Pseudomonas aerugenosis #1	Pseudomonas aerugenosis	Mandelamine
	10,000	Pseudomonas aerugenosis #2	Proteus rettgeri	Ascorbic acid
	20,000	Alpha Streptococcus enterococcus	Mima polymorphia	
Feb. 1973 (2 weeks later)	100,000	Proteus rettgeri #1, #2	Proteus rettgeri	Mandelamine
	1,000	Pseudomonas aerugenosis	Proteus morgani	Ascorbic acid
			Proteus mirabilis	

TABLE 6

Date	Ileal Loop Urine Culture Colonies/M1.		Stoma Swab Culture	Treatment
Apr. 1972	40,000	Enterobacter	Enterobacter, Providence Proteus mirabilis, Escherichia coli Alpha Streptococcus enterococcus	Macrodantin
June 1972	1,000	Pseudomonas aerugenosis		Macrodantin
July 1972	20,000	Pseudomonas aerugenosis	Pseudomonas aerugenosis	Gantanol
Oct. 1972	90,000	Citrobacter diversus	Pseudomonas #1, #2	Gantanol
	30,000	Citrobacter diversus #2	Escherichia coli #1, #2	Macrodantin
			Alpha Streptococcus enterococcus	
Jan. 1973	50,000	Pseudomonas aerugenosis	Gamma Streptococcus	Ampicillin*
			Corynebacterium	Gantanol
Mar. 1973	100,000+	Citrobacter diversus	Citrobacter diversus	Gantanol
	2,000	Citrobacter diversus #2	Klebsiella, Escherichia coli	
	8,000	Pseudomonas aerugenosis	Proteus mirabilis	
			Alpha Streptococcus enterococcus	

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*Prescribed for respiratory infection.

fore becomes difficult to set a standard criterion to differentiate between contamination, transient and true bacteriuria.

Tables 2-6 illustrate examples of variation in concentration of the same species of organisms found in follow-up cultures although it is impossible to state definitely that the organisms recurring in follow-up cultures are the same strain, it seems likely that they represent a continuation of the same infection.

Frequently it appears one species has been eradicated, while another emerges often necessitating treatment with more than one antibiotic. Gracey, et al.[11] has shown morphological changes in the mucosa of the ileum after conversion to ilial conduit for urinary diversion and reported that the possible role of altered bacterial flora of the conduit in the etiology of these morphological changes merits consideration. The pathogenesis of the morphological changes is unclear. Minton, et al.[12] has reported evidence that patients with ileac diversions develop reflux within about four months after surgery. The effect of bacteria in the refluxed urine on the kidney cannot be overlooked.

The first of the three questions motivating this study has been partially answered: the use of the telescoping double lumen catheter for obtaining specimens for urine culture is of great use in differentiating contamination from true bacteriuria.

Much more investigation is needed to provide definitive answers to the other two questions:

1. Is the incidence of positive urine cultures in spinal cord-injured patients with ileal diversions due to continuing infections or new infections?
2. What are the sources of these infections?

When these questions are answered, the approach to the level of bacterial concentration which indicates treatment will become more rational.

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I am compiling case reports of allergic reactions to biting insects, i.e., mosquitos, fleas, gnats, kissing bugs, bedbugs, chiggers, black flies, horseflies, sandflies, deerflies, etc. I am also interested in reactions to the Imported and Southern Fire Ants.

Physicians please mail me case reports of those patients who have had reactions to such insects. Include in your reports, the type of reaction and the complications, if any, the age, sex, and race of the patient, the site of the bites, the season of the year, the immediate symptoms, the skin test results, desensitization results, if any, and any associated other allergies. Send this information to the following address: Claude A. Frazier, M.D., 4-C Doctor's Park, Asheville, NC 28801.

Scar Revision

ROBERT H. MATHOG, M.D.*

Although most abrasions, contusions, and lacerations of the face will heal with no scar, there will always be a small group of individuals who will develop some deformity. The cosmetic problem may be that the scar is excessively wide, contracted, deep, hypertrophied, or angulated. In most cases, treatment will consist of a revision of the scar tissue timed to coincide with maturation of wound healing. This will involve camouflage techniques such as excision, transposition of tissues and "breaking" the scar line. Knowledge of these principles of scar formation and revision will assist in early care of the wound and the counseling of patients desiring correction of deformities.

THE FORMATION OF scar is a natural process resulting from skin injury. Whenever skin is disrupted through all layers, there is a proliferation of fibroblasts and a deposition of collagen forming the so-called scar. Sometimes the scar falls into a natural crease or shadow which creates little if any deformity. Often the scar is thick, crosses crease lines, disturbs symmetry and creates a cosmetic defect. It is this deformity that needs to be evaluated, and if desired, corrected by modern surgical techniques.

Skin Injury

Skin can be injured by many forms of trauma: heat, cold, chemicals and sharp or blunt penetrating objects. The extent and depth of injury will determine whether the injury is classified as an abrasion, contusion, laceration or avulsion.[1]

Abrasions occur as superficial injuries involving only the epidermal or outer dermal areas. The basal layers of skin remain intact. Occasionally this form of injury may entrap foreign material into the skin substance, creating a permanent tatoo; however, if the wound is kept clean, most abrasions heal quickly without any permanent sequelae.

Contusion characterizes an injury of a deeper layer of tissue. Here a blunt object causes rupture of deep vascular elements with the ultimate formation of hematoma. The hematoma may press against the skin creating a pressure that may devitalize superficial layers. Nonetheless, in most cases, the skin usually remains intact and the healing is uneventful.

Lacerations almost always produce a scar. Penetration of all layers of skin by a sharp or blunt instrument creates the laceration which heals by scar tissue formation. Often there is an associated contusion and abrasion. It is possible for lacerations to enter deeper areas and destroy vessels, nerves and muscle tissues.

The avulsion, another type of common injury, may also result in scar formation. In this form of injury, there is a loss of tissue created by a shearing force against the skin surface. Whether treated by local flaps or by skin grafts, this injury will eventually produce a scar. Loss of subcutaneous or deeper tissues often results in depression of the scarred area.

The other type of injury, the puncture wound, usually occurs in combination with lacerations and avulsions. Frequently the puncture wound can be very small and cause no cosmetic deformity. Larger wounds, such as seen with gunshot injuries, may be associated with a great deal of scar formation and later present with a severely deforming appearance.

Wound Healing and Scar Formation

Usually the lacerations, abrasions and puncture wounds are associated with separation of skin. It is here that there occurs a process natural to all injury that proceeds to heal the wound. This involves a series of complex biochemical, cellular and mechanical events which close the wound[2] and may or may not produce the unsightly scar.

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There are essentially three phases of healing as outlined in Table 1—the substrate, proliferative, and resorptive phases. Since they serve as a part of a continuum for wound healing, they tend to overlap and are difficult to distinguish from one another.

The substrate phase is observed during the first three to five days after the injury. It is characterized by fibrin formation which initially holds the wound edges together. Examination of tissues demonstrates a thrombosis of vessels, plasma collection and a preponderance of leukocytes.

The proliferative phase develops at about the third to fifth day and lasts for approximately two weeks. During this time, fibroblasts appear in the fibrinous material and there is an initiation of collagen synthesis. Wound strength increases and epithelial cells proliferate across the wound surface. Thus, wounds obtain about 25 percent holding strength or just enough to maintain a closure of the wound without sutures. Any scar appearing at this stage is red and firm.

Following the proliferative stage, healing of the wound enters a third or resorptive phase. The fibroblasts and capillaries disappear and young collagen is resorbed. The older collagen becomes more oriented, later creating a contracture of the tissue. As the wound becomes smaller, the strength increases. Maturity is indicated by a change of color of the wound from pink to white. At the end of this stage the scar has become stabilized and is best suited for evaluation and revision.

Scar Appearance

The scar that develops following injury and wound healing can be classified according to three basic components: line, contour and color.[3] All of these factors give the scar certain characteristics which distinguish one type of scar from another. This becomes important in the evaluation of the scar and subsequent treatment.

The line of a scar may be fine, wide, long or broken. Usually the fine scars are those that have developed from clean cut lacerations with little or no infection. Wide scars often indicate that there has been some degree of separation of the wound either from skin tension in opposite directions, infection or other processes that can delay healing.

The contour describes the elevation of the scar in relation to adjoining structures. Other terms useful in describing contour of a scar are depression, contraction, elevation, hypertrophy and keloid. Scars below the surface indicate some loss of supporting tissue while those extending above the surface suggest some degree of over-activity in the healing process. It is well know that adverse local factors such as wound tension, infection and secondary healing create the hypertrophic-keloid scar,[4] but it is poorly understood why this occurs in some individuals, and yet under the same apparent conditions, is absent in others.

The color usually defines the age of the scar. The young scar is red or pink, and as the scar matures, the color whitens and becomes less obvious. This color change may take from six to 18 months after the injury. Adverse pigmentation may occur in some scar if there has been insufficient debridement of the wound at the time of initial injury.

Scar Revision

The basic goal in scar revision is to camouflage the obvious scar. In order to successfully accomplish this, it is necessary to understand what types of scars are ugly and what scars are cosmetically acceptable. It is also important to know if it is technically possible to convert an obtrusive scar into one that is acceptable to the patient.

There are several guidelines that govern scar revision.[3,5,6] Wide scars should be narrowed, assuming they will not create a disturbance of adjoining tissues, i.e., eyelid or corner of the mouth. Long scars (greater than 2 cm) should be broken

TABLE 1
Phases of Wound Healing

Phase	Approximate Days	Cellular Activity	Environmental Activity	Wound Appearance
Substrate Phase	0-5	Leukocytes Red blood cells	Plasma	Fibrinous exudate
Proliferative Phase	5-20	Young fibroblasts Vessels Epithelial cells	Collagen formation	Red, firm scar
Resorptive Phase	20-180	Mature fibroblasts	"Tightening" of collagen	White, contracted scar

o prevent easy visualization. Scar angulation from kin creases should be converted to scars in the natural crease or shadow. Depressed scars should be elevated, while hypertrophic or keloidal scars educed to provide a smooth surface. Contracting cars should be lengthened to release the tension of adjoining structures.

Some of the techniques used in bringing about hese corrections vary from surgeon to surgeon. Often they will depend upon the requirements of the patient rather than the lesion itself. There are certain principles which in most cases will provide an acceptable result—a concealed non-deforming scar. These include basic methods of anesthesia, tissue handling, sutures, and dressings in addition to specific camouflage techniques.[7,8,9,10]

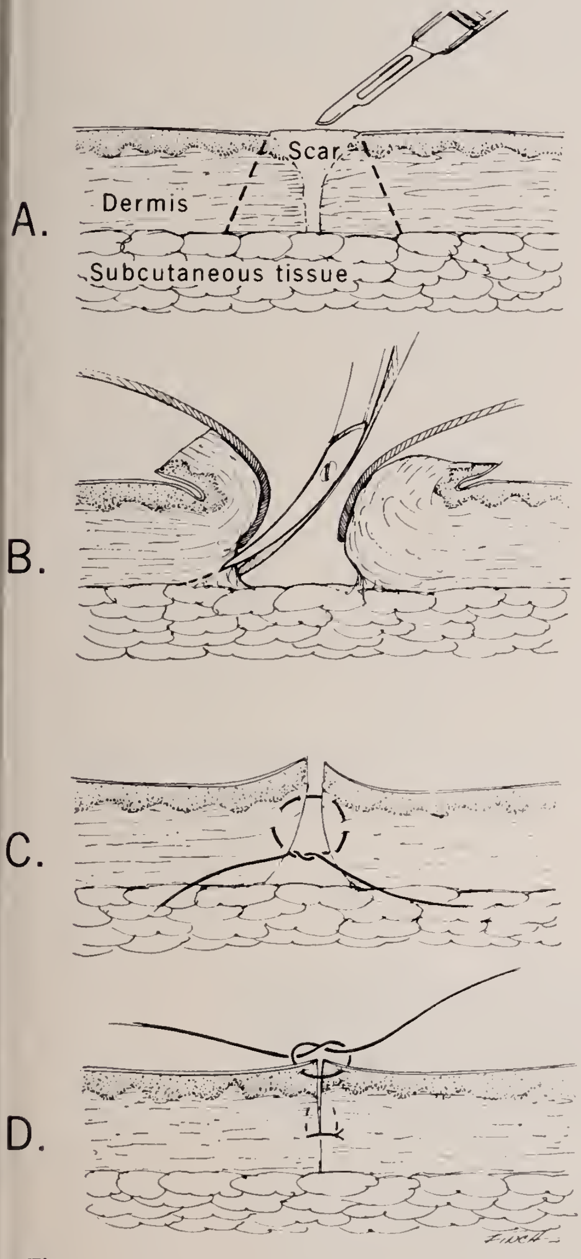

Fig. 1—Techniques of skin incision and closure. A. Beveling of the incision. B. Undermining of subcutaneous tissues. C. Closure of the dermis (subcuticular sutures). D. Closure of the skin.

Basic Techniques

Although one must consider the patient's desires and general condition in selecting the anesthesia, it is advisable to employ local hemostatic agents. This will control bleeding and the surgery will usually progress with minimal difficulty. For most procedures Xylocaine containing 1:100,000 epinephrine is sufficient. Vasoconstrictive effects will occur at about ten minutes; thus any skin incisions should be delayed for this amount of time.

Skin incisions are usually made at right angles to the skin and/or beveled slightly away in anticipation of a closure with eversion (Figure 1). The incision is carried down to the appropriate subcutaneous plane whereupon the skin is undermined in all directions. This tends to relieve tension in the ultimate closure of the wound. Trauma to the skin edges is avoided by the gentle use of sharp hooks. Hemostasis is maintained with pinpoint cauterization of small vessels.

In closing the wound different suture materials are available. Needless to say, the first sutures are placed in a subcuticular or dermal plane to relieve the tension from the superficial cutaneous layers. Popular suture materials are relatively inert and cannot be seen through the skin. They are usually braided white or colorless fibers such as polyester (Mersilene or Dacron). The skin itself is closed with a fine cutting needle and non-absorbable, non-reactant materials such as monofilament nylon (Dermalon) or polypropalene (Prolene). Interrupted or "running baseball" sutures applied to the wound, equidistance from the edges as well as from each other, can be used to approximate the tissues. Occasionally rubber bands are employed as drains to control bleeding or a dead space.

Most facial wounds are also treated with a dressing. This serves to stabilize the wound and place it at rest. The dressing absorbs the wound discharge and maintains a moist surface for optimal epithelization. It also reduces swelling and provides pressure for additional hemostasis. Dressings are made bulky to create even pressure, but small wounds may be treated with a more conservative "colloidin" type of surface splint.

Specific Techniques

The usual techniques in correcting common scar problems are noted in Table 2. These camouflaging methods include variations on Z-plasty, broken line techniques, skin grafts and steroid injections.

TABLE 2
Scar Revision

Scar Deformity	Requirement	Technique
Width	Narrowing	Excision
Length (greater than 2 cm)	Breaking the line	Z-plasty, W-plasty, Zigzag plasty
Angulation	Changing the crease line or shadow	Z-plasty
Depression	Elevation	Z-plasty or advance of subcutaneous tissues; autogenous implant
Hypertrophy and Keloid	Depression and narrowing	Steroid injection or excision
Contracture	Lengthening	Transposition with Z-plasty; mucosal or skin grafts

Excision

The revision of most facial scars requires an excision of scar tissue. If the scar is in a shadow or crease line, excision is all that may be necessary to conceal the defect (Figure 2). Crease lines are similar to relaxed skin tension lines* and because of less tendency to widen, scars in these areas provide a good cosmetic result.[11]

Occasionally excision of the scar is associated with a loss of tissue. In these cases local flaps or skin grafts are necessary to close the defect and minimize contracture. This is especially true for scars associated with a loss of tissue near the mouth, eyelids or neck areas (Figure 3).

When contracture is not a problem, and yet the scar is excessively wide, the deformity can be corrected in stages.[12] Certain areas such as the cheek and neck, where the skin is loose, can be mobilized for a partial excision of the scar. This is repeated on different occasions until the scar is completely excised.

Z-Plasty

Often a scar is angulated to a creaseline, and contracts and distorts facial features (Figure 4). In such cases, it is necessary to change the orientation and lengthen the line of the scar. This is best accomplished by Z-plasty techniques utilizing a transposition of two triangular flaps.[13] In es-

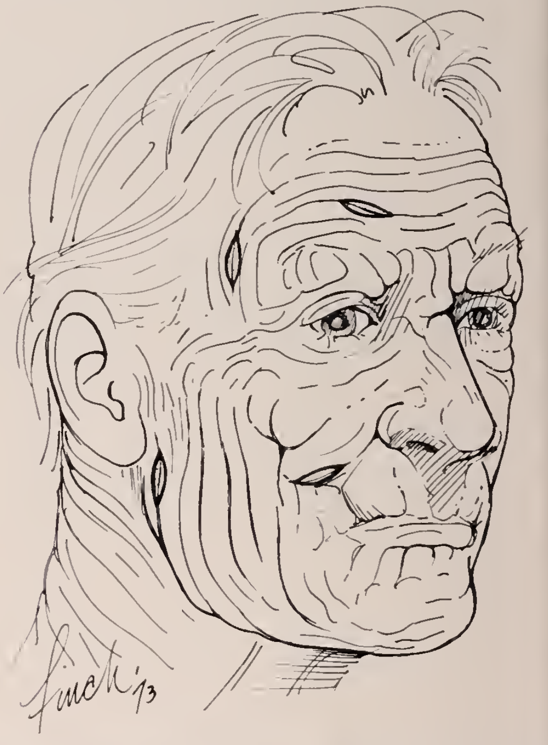

Fig. 2—Natural crease lines of the face and typical excisions.

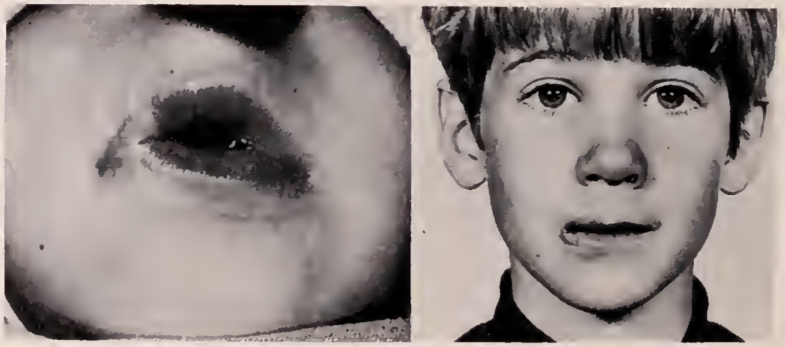

Fig. 3—Electrical burn of the lip demonstrating severe contracture and correction by excision and advancement of local mucosal flaps.

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*Skin creases should not be confused with Langer's Lines which were initially demonstrated on cadavers and do not necessarily represent lines of least tension.

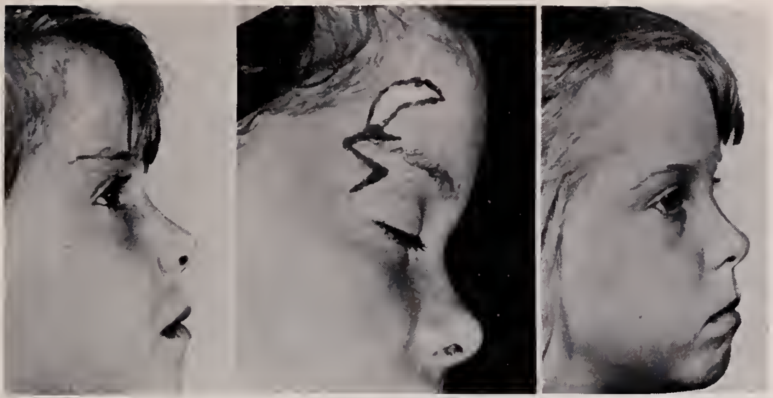

Fig. 4—Wide scarring and contracture of the upper eyelid. Correction by excision and Z-plasty.

ence, the Z-incision describes two of the sides nd a diagonal of a parallelogram (Figure 5). Vith a transposition of the triangles, the diagonals nd arms are rotated into a new position. The mount of lengthening of the diagonal will depend pon the angle of the Z. At angles of 60 degrees, here is a 75 percent increase in the line of the diagonal of the Z. At 45 degrees there is a 50 percent increase and at 30 degrees only a 25 percent increase in this same diagonal. In practice the most useful angles are from 20 to 60 degrees.

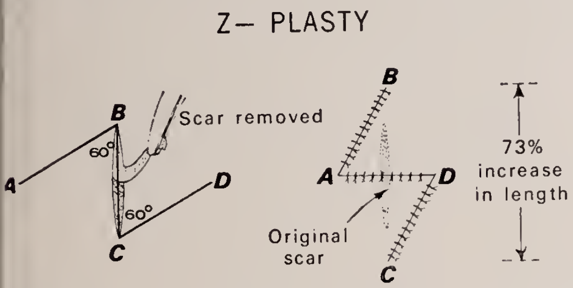

Fig. 5—Z-plasty. Lines A,B,C,D, define a Z. The otted lines help to describe a parallelogram with a digonal B,C. Upon transposition of the flaps B to D and C to A, a lengthening is noted in B-C at the expense of A-D. The difference between the two diagonals is the mount of relaxation.

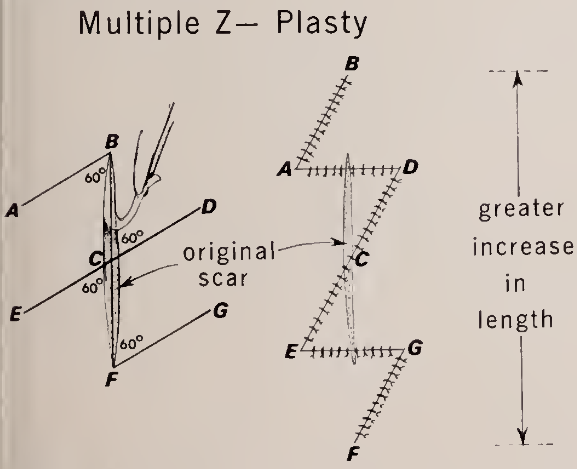

Fig. 6—The multiple Z-plasty. Lengthening is greater than 75 percent noted in the Z-plasty of Figure 5.

Obviously there is a limit to the amount of lengthening in one Z maneuver. Additional length can be obtained however, by multiple Z-incisions[14] (Figure 6). These techniques are useful when they are applied to scars in hidden areas, but the repeating form of the scar makes it less desirable for use on the face.

W-Plasty and Zigzag Plasty

Many of the scars of the face are long (greater than 2 cm) and therefore conspicuous. Dividing the scar into smaller ones of different directions, camouflages the original scar making it difficult to visualize the entire line (Figure 7). Moreover, multiple smaller scars lengthen the total scar line avoiding contracture. These techniques are actually modifications of the Z-plasty principle and are described by the W-plasty and zigzag plasty methods.

The W-plasty is created by excising the scar with small regular continuous W-incisions so that they ultimately interdigitate with one another. The zigzag-plasty attempts to reduce the regularity of the scar by mixing the W-incision with small triangles and squares. Although there is always

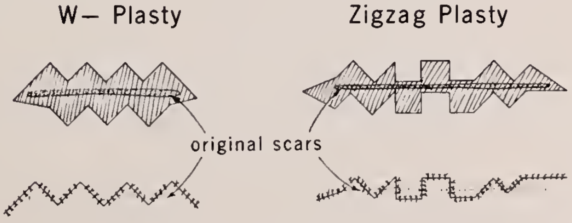

Fig. 7—the W-plasty and zigzag plasty excision.

a preference for the incision lines to follow crease lines, they also must be made to interdigitate with one another. These camouflage techniques are best suitable for large scars of the face crossing smooth areas such as the cheek (Figure 8).

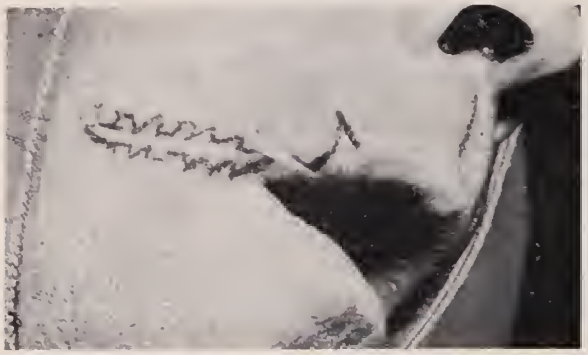

Fig. 8—Correction of cheek scar by zigzag-plasty technique.

Depressed Scars

Occasionally a scar is noticeable because of an associated large depression. When this occurs, the scar is excised utilizing one of the aforementioned techniques. Often simple transposition of tissues will reduce the deficit. When more is necessary the subcutaneous tissues can be advanced by sliding or transposition flaps. Sometimes the subcutaneous tissues can be increased with the addition of dermis, fat, muscle and cartilage grafts.[3] A bunching of the dermal layers and eversion of the skin edge can also help to obliterate the deficit.[8]

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Cover Photo

"Winter Wonderland"

Dr. John E. Lonstein, who claims to be an amateur photographer, took the cover photo during the winter of 1972 in Eloise Butler Park, a small park in Minneapolis. It was one of the very few occasions that the snow still clung to the trees after a heavy snowfall.

Born in South Africa, Dr. Lonstein obtained his medical education from the University of Witwatersrand in Johannesburg in 1964. He later did a two-year general surgical residency training at the Boston University Medical Center under Dr. Richard Egdahl, a graduate of the University of Minnesota Medical School. Becoming interested in orthopaedics, Dr. Lonstein moved to Minnesota where he did a residency under Dr. John Moe at the University of Minnesota. After completing his residency, he became an instructor in the Orthopaedics Division of the Department of Surgery at the University of Minnesota, and a member of the Twin Cities Scoliosis Center.

Dr. Lonstein enjoys photography and excells in scenery, architectural, outdoor and family photographs.

Letter to the Editor

Dear Editor:

This is written in reference to the editorial by Dr. Monahan* in the October issue.

Dr. Monahan, in discussing physicians assistants states that "Despite the rejection of the physician's assistant by organized nursing, nursing support is surprisingly good (90%)". Would Dr. Monahan identify his statistical source for 90% and also clarify the base i.e., 90% of what nurse population? Nurse practitioners? Educators? Active or inactive nurses? etc.

The statement about organized nursing's resistance to delegation by physicians is inaccurate. The Minnesota Nurses Association has never opposed the physician's right to delegate—in fact in our testimony at the Minnesota legislature we have supported that right.

The Minnesota Nurses Association has however repeatedly testified to its concern that the proposed language of the bill has consistently given broad latitude to the physician to delegate anything to anyone. It is our contention that such a broad delegatory statute does not insure the patient that *only* persons adequately trained and supervised will be doing that delegated task or function.

We recognize that by far the majority of physicians would delegate judiciously and not risk allowing improperly trained "assistants" to give care to a patient. Nevertheless, the purpose of the law is to protect the public. It is our position that giving broad delegatory statutory authority without some criteria for education, training, supervision and areas of limitation allows potential for indiscriminate use of that authority. Therefore such provision would not, in fact, safeguard the quality of care to the people.

I wish to respond to the question in the editorial: "If 90% of the nurses recognize that delegation by physician's assistants is beneficial to the patient and to the health care system why is organized nursing so unresponsive to its constituents by condemning delegation to physician's assistants?" My comments are:

1. Organized nursing does not object to physicians assistants if they are, in fact, prepared, trained and supervised by physicians to do *medical acts*, tasks and functions.
2. Organized nursing does object to using nurses as physicians assistants dependent upon the physician to do only delegated technical medical acts, tasks or functions. It is our belief that the nurse who goes this route is not practicing nursing, but is in "limbo" between medical and nursing practice.
3. Organized nursing believes that the quality and availability of health care to people can be enhanced (and the physician's knowledge and skills better utilized as well, if there were an increase in the number of nurses prepared to function in an expanded nursing role. This involves health care supervision, teaching, counseling, assessment of health or illness needs and independent *nursing* judgments. In Minnesota, the U of M School of Public Health Nursing prepares such nurse practitioners to function in pediatrics, geriatrics and adult health. The University of Minnesota School of Nursing has Master's programs in medical, surgical, psychiatric and maternal-child health nursing.

   These nurses function under their own professional accountability and in this way help to expand the scope and availability of health care. They make nursing assessments and work collaboratively with physicians and other professionals in the health team to provide the full range of services needed.

Ruth M. Lunde
Executive Director
Minnesota Nurses Association

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*The Physician's Assistant versus the Nurse Associate, Minnesota Med October, 1973, p. 877.
(Ms. Lunde's letter was sent to Dr. Monahan whose reply is on Page 38.)

Letter to the Editor (Continued)

Dear Editor:

Ruth M. Lunde, Executive Director of the Minnesota Nurses Association, in criticism of my editorial "The Physician's Assistant versus the Nurse Associate" says:

"Dr. Monahan, in discussing physician's assistants states that 'Despite the rejection of the physician's assistant by organized nursing, nursing support is surprisingly good (90%).' Would Dr. Monahan identify his statistical source for 90% and also clarify the base i.e., 90% of what nurse population? Nurse practitioners? Educators? Active or inactive nurses? etc."

I refer her to the source material of my editorial. I was asked to discuss two specific articles, Ms. Lunde apparently read only one. I refer her to Doctor Gonzalez's article in Minnesota Medicine, Section 2, page 66, October, 1973, the second article that I was asked to discuss. Paragraph 2, line 7: "Contrary to *rejection of the physician's assistant concept by organized nursing,* 90% of the nurse respondents felt that the physician's assistant would fill a need in health care delivery; . . ."

Ms. Lunde also states:

"The statement about organized nursing's resistance to delegation by physicians is inaccurate. The Minnesota Nurses Association has never opposed the physicians right to delegate—in fact in our testimony at the Minnesota legislature we have supported that right."

On page 66 of the Minnesota Medicine supplement under the *Problem of Legal Delegation,* Doctor Gonzalez discusses the Minnesota State Medical Association's attempt to introduce a delegatory amendment to the Medical Practices Act in 1972. I quote from paragraph 1, line 5 of the same article (page 67) "Pharmacy, Nursing, and Optometry strongly opposed the delegatory bill . . ."

By quoting from the source I do not retreat from the position of my editorial; rather I wish to emphasize that I strongly support the position taken by Doctor Gonzalez.

It is my personal opinion that Ms. Lunde's statement "The Minnesota Nurses Association has never opposed the physician's right to delegate"—is incorrect. It is the hyperbole of misstatement. Organized nursing not only failed to support medicine but was actually antagonistic on the subject of the physician's right to delegate. The fact that the nurses joined optometry and pharmacy in a parade on the State Capitol to oppose the Bill sponsored by the Minnesota State Medical Association is evidence enough.

Mr. Lunde's final statement is that she wishes to respond to the question "why is organized nursing so unresponsive to its constituents by condemning delegation to physician's assistant"; it appears that her three responses are merely apologetics for why they *do* object to delegation.

Three phrases stand out in a review of her letter:

1. "—a law to protect the public."
2. "—an expanded nursing role."
3. "—function under their own (nurses) professional accountability—."

That these concepts occur here as they do in so many other "professional" publications suggests that we are here dealing with yet another self-interest group looking for what it considers to be a piece of the action.

Robert Hugh Monahan, M.D.
President
Joint Commission on Allied Health Personnel in Ophthalmology

The patient with asthma or allergy: another type for Tylenol® (acetaminophen)

When the allergic patient has a condition requiring an analgesic, a new problem arises. "Idiosyncrasy to salicylates is not rare and is usually manifested by skin rashes and anaphylactoid reaction. Sensitivity to these drugs occurs more frequently in patients with asthma and allergy."[1] Moreover, the previous ingestion of aspirin without ill effects is no guarantee that subsequent use will not precipitate a severe reaction.[2]

TYLENOL (acetaminophen), on the other hand, presents little risk of allergic reaction, even in patients sensitive to aspirin,[3] making it the preferred analgesic for the allergic patient.

This is only one of several 'types for TYLENOL'—that is, patients who should avoid aspirin. Considering all of them, wouldn't it provide added safety (as well as added convenience) to recommend TYLENOL (acetaminophen) routinely for simple analgesia?

References: 1. Modell, W., ed.: Drugs of Choice 1970-1971, St. Louis, The C. V. Mosby Company, 1970, p. 196. **2.** Goodman, L. S., and Gilman, A., ed.: The Pharmacologic Basis of Therapeutics, ed. 4, New York, The Macmillan Company, 1970, p. 327. **3.** Maslansky, L. Paper delivered at Fourth International Congress of Allergology, New York, Oct. 18, 1961 abstracted Excerpta Med. Internat. Congress Series, No. 42, p. 124.

Precautions and Adverse Reactions: If a rare sensitivity reaction occurs, the drug should be stopped. TYLENOL (acetaminophen) has rarely been found to produce any side effects.

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These same characteristics make Lomotil useful in controlling the diarrhea associated with gastroenteritis, antibiotic therapy and acute infections.

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Telegram

IMPORTANT INFORMATION: *This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.*

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: ***Lomotil is contraindicated in children less than 2 years old.*** Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

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Editorials

Lung Cancer Surgery

JOSIAH FULLER has made an important contribution in his paper, Surgical Treatment of Lung Cancer.* It is obvious that he is well acquainted with this disease and the problems that it presents. That he has utilized the available surgical armamentarium with discretion and skill is apparent from the five-year survival statistics. He has clearly reached his objective of illustrating that for those patients in whom resection is possible, the outlook for "cure" is not entirely dark.

We would emphasize his point that the histologic diagnosis of small cell carcinoma is occasionally not reliable. This is particularly true when diagnosis is based on frozen section. In such cases clinical evidence must be considered, and no patient denied resection solely on the basis of the pathologist's report.

It apparently was beyond the scope of the article, but we would be interested to know the size of the patient pool from which these operable cases were chosen, and the criteria used in deciding operability. The article was not clear as to whether the node involvement referred to was lobar hilar, pulmonary hilar on mediastinal. There are also questions about how anterior mediastinotomy was used in determining operability and what, if any, place scalene node dissection played in this decision.

In our own practice we feel that positive mediastinal nodes should not exclude the patient from operation, particularly for a right sided lesion, where very thorough mediastinal node dissection is part of our standard procedure for lobectomy or pneumonectomy. Carcinoma of the left lung may be judged inoperable if mediastinal nodes are positive because of the technical difficulty of performing an adequate mediastinal dissection from the left side. The scalene nodes are the first group beyond the reach of our intrathoracic dissection and even though they are not palpable on physical examination, these nodes have been found to be positive in approximately 20% of cases of lung cancer. Bilateral scalene node dissection is considered to be important in the preoperative assessment of patients with carcinoma of the right lung particularly. Mediastinoscopy has a role in assessment of patients with carcinoma of the left lung. Patients with positive scalene nodes are incurable by even the most enthusiastic surgeon.

Dr. Fuller's article deserves attention for focusing on one of the brighter spots in our continuing battle with this disease.

Frank E. Johnson, M.D.
Minneapolis, Minnesota

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*Minnesota Med 56:1024, 1973.

Minnesota State Medical Association

121st Annual Meeting of the Minnesota State Medical Association will be held in Duluth, May 16 and 17, in the Duluth Arena-Auditorium.

Endotracheal Intubation of the Newborn

The article by Dr. Strickland* demonstrates a deep understanding of the problems of establishing and maintaining an airway in small infants. Her emphasis on competent and conscientious care in newborn problems has made her a leader in the field.

The need for ventilation in infants with respiratory failure cannot be emphasized too strongly. The problems of intubation have been well defined in the paper. The child is small, and the relative location of the trachea is different. Intubation of the esophagus by mistake can happen. The tissues of the esophagus are fragile, giving rise to possible hemorrhage, ulceration or necrosis. The tube itself must be secured well or it may slip out or slide down into a main stem bronchus.

There is no doubt that this technique of endotracheal intubation for respiratory support is effective and safe in capable hands.

There are bag and mask systems available which are effective approximately 90% of the time. The technique can be learned with just a few minutes practice. One does wonder about the physician who is called upon once or twice a year to give positive pressure assistance to an infant, if this technically less difficult system should not be the first line therapeutic measure.

Of course, there is this small group of patients who do not respond to bag and mask assistance. The practitioner should then resort to endotracheal intubation as it is artfully described by Dr. Strickland.

David B. Klain, M.D.
Children's Health Center

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*Minnesota Med 56:8:703, 1973.

Snowmobiling

Dr. Karleen,* in his article "Snowmobiling with Associated Maxillofacial Injuries," has thoroughly reviewed the literature on this rather recent problem. His study of patients with maxillofacial injuries who received care at the major hospitals of suburban Minneapolis during 1969 is complete and timely.

Most informative is the tabulation of the types of injuries incurred and the mechanism of the injury. This type of information is needed to promote action by the legislatures to develop sensible laws to regulate snowmobile use.

A Summary of this work was presented in the Minnesota Department of Natural Resources bulletin—"Conservation Volunteer"—where it is available to non-medical readers. A compilation of this type of information should be of great value to the manufacturers of the snowmobile who are interested in improving their designs to make safer machines.

Lyle V. Kragh, M.D.
Minneapolis, Minnesota

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*Karleen CI: Snowmobiling with associated maxillofacial injuries. Minnesota Med 56:975, 1973.

Osteoporosis

Dr. Won Savage* has studied the recording of the diagnosis of primary idiopathic osteoporosis in a voluntary hospital. The low incidence of formal recording of this diagnosis, 27 out of 9,316 admissions, certainly must be exceeded many times by the radiologic observation of demineralization of the central skeleton. One would assume that radiologic indication of the disease often does not find its way to the record room and to the PAS recall mechanism, probably reflecting its lower priority in the medical diagnostic hierarchy. Bone mineral analysis, (such as the Cameron photon absorption technique), is precise and readily available commercially and has not found wide application clinically, probably also reflecting relatively low status. Dr. Won Savage's summary is an interesting overview of practice in regard to this diagnosis.

Stanley C. Von Drashek, M.D.
Abbott-Northwestern Hospitals

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*Minnesota Medicine 57:1027, 1973.

Postural Screening

The relationship of human posture and many of life's processes have been investigated for many years. So-called "faulty postures" in infants have been examined for clues to idiopathic scoliosis. Lateral asymmetries of posture in youth may be progressive in nature thereby contributing to abnormal dynamics of adult vertical alignment. The functions of various organ systems have been monitored while humans have been sitting, standing, and reclining.

The article "Postural Screening," by Dr. Maloney, et al.* presents an informal approach to the detection of abnormal posture in grade school children. While the study is informative, the method described notes the failure to assess variability of evaluation between therapists, and the lack of photographs, Xrays, or measurements. The use of questionnaires, with data that was not validated, did not appear helpful to the examiners. The degrees of postural deviations given as "mild," "moderate," or "severe" seemed vague, urging more specific and definitive measurements. While the authors conclude that the cost of such a screening clinic is prohibitive, suggestions for future economic alternatives need appraisal.

The many unanswered questions raised by this informal study suggest a need for further assessment of posture in school age populations. Such a study might involve other elements possibly relating to posture, such as body type, family constellation, environment, physical activities, and nutrition. Future conclusions about postural variations should be fully supported by statistically significant findings. Comparisons of such variations with those of other studies, of greater depth and longer follow-up, would be valuable.

W. J. Dawson, Jr., M.D.
Minneapolis, Minnesota

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*Maloney FP and Hildebrandt Sharon: Postural screening in an elementary school. Minnesota Med 56:1075, 1973.

Urinary Tract Injuries

Management of injuries to the urinary tract is well outlined by Drs. Ireland and Cass. It is noted that a large percentage of their patients, as described in both the present essay and in previous ones, have associated intraperitoneal injuries which have required immediate exploration and treatment. During the course of surgery, injuries to the urinary tract have been observed and treated effectively. The need for urgency in event of damage to the renal pedicle is accepted, but when the damage is parenchymal, many urologists are inclined to allow the condition of the patient to become stabilized before determining whether a surgical procedure is indicated. It is not unusual for both the excretory urogram and the angiogram to demonstrate abnormalities, only to note a normal appearance of the injured kidney on subsequent studies; thus the need for surgery upon an extremely injured patient might be averted. Ureteral injuries, unless associated with intraperitoneal trauma, are rarely rocognized immediately, but fortunately respond well to treatment after suspicion of their presence leads to retrograde ureterography.

Most bladder injuries are secondary to pelvic fractures which are productive of extensive perivesical and dissecting retroperitoneal blood accumulation. Intraperitoneal lacerations require early closure, but in approaching extraperitoneal leakage or transections of the urethra one must be prepared to combat a signficant loss of blood during the course of repair. A calculated risk of infection exists when one chooses to treat these patients conservatively, but with careful observation this course might be preferable. A seemingly benign situation exists among patients with wide symphyseal separations, but in our experience about one half of them have linear lacerations of the membranous urethra, giving rise to eventual sepsis.

The improvement in diagnostic methods, which has evolved during the last few years, has made possible precise assessments.

Richard S. Rogers, M.D.
Minneapolis, Minnesota

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*See page 15.

Membrane Oxygenator

PROLONGED EXTRACORPOREAL oxygenation is being used in the treatment of an increasing number of patients in acute respiratory failure.* To date there has been a survival rate in the range of 10-20% in this group of extremely ill patients. As with other developing forms of therapy, more experience must be gained to clarify the indications for its application. The technical aspects of establishing and maintaining extracorporeal oxygenation have long been available but today improved materials and membrane oxygenators have made more prolonged periods of support feasible. The hazard of uncontrollable bleeding remains a major deterrent to the widespread use of this technique.

What are the criteria for establishing extracorporeal oxygenation? First all conventional modes of therapy should be exhausted. These include maintenance of a patent airway, mechanical ventilation, fluid restriction, diuretics and antibiotics where appropriate. Particularly indicated in circumstances of acute respiratory failure is the application of a positive end-expiratory pressure (PEEP). Only after failure to respond to these measures should extracorporeal oxygenation be considered. An impartial evaluation by physicians not involved in the care of the patient should be sought in order to assure that the rigorous criteria for this mode of therapy are fulfilled and to assess the reversibility of the disease process.

With additional experience the technique of extracorporeal oxygenation should provide a superior form of treatment for patients in acute respiratory failure who currently succumb to potentially reversible pulmonary diseases.

Alan D. Sessler, M.D.
Section of Respiratory Intensive Care
Mayo Clinic

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*Spenny E et al: Respiratory failure in influenza pneumonia treated with membrane oxygenator. Minnesota Med 56:1017, 1973.

It's the Law

Res Ipsa Loquitur Applied in Spinal Anesthesia Case

The doctrin of res ipsa loquitur was applicable in a case of alleged injury from spinal anesthesia. The patient underwent spinal anesthesia for correction of a hernia. At the time of insertion of the spinal needle, he felt a strong electrical current through the lower half of his body. Following the anesthesia he had no sensory perception in the entire lower half of his body from the naval downward.

Even though no specific testimony was introduced which would indicate wrongful act, the court ruled that the fact that he had total sensory loss following the spinal anesthesia was sufficient in itself to indicate an inference of negligence. The patient was awarded damages for the injury.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Younger v. Webster, 510 P.2d 1182 (Wash. Ct. of App., June 6, 1973) The Citation 28: 2, November 1, 1973.

Falstaff: A pox of this gout! or, a gout of this pox! for the one or the other plays the rogue with my great toe.*

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*Shakespeare, 2 Henry IV I.ii. c. 1600.

Special Article

Use of Anti-D (RhoGAM) to Prevent Erythroblastosis Fetalis

JON F. BERLAUK*

Currently RhoGAM is not suggested for the treatment of an Rh negative patient transfused with Rh positive blood by mistake. McElrath et al.[10] have used it for this purpose, and with good results. While this promises to be another potential use, further study is necessary.

When Levine et al.[18] first described the common pathogenesis of erythroblastosis fetalis, congenital anemia, severe icterus and hydrops fetalis in 1941, these diseases constituted a significant percentage of infant morbidity and mortality. Rh hemolytic disease (erythroblastosis fetalis) is one of the most common genetic pathologies among Caucasians, occurring in greater than one in 200 births.[19] At present between 300,000[7] to 400,000[17] women are at risk of developing Rh immunization in the U.S. approximately 13% of all marriages.[4] Of these women at risk only 6%[19] to 10%[7] will actually become immunized.

Erythroblastosis fetalis occurs because the infant's red blood cells contain an Rh (D) antigen which the mother's red blood cells lack. She will make antibody (IgG class) to this Rh antigen once she has been exposed. The disease normally does not affect the first infant with Rh positive blood since fetal blood cells enter the maternal blood stream mostly during delivery, and it takes about 16 weeks for the mother to develop antibodies against these cells.[7] It is normal for some fetal cells to enter the maternal blood stream during early fetal life. 4% to 10% of mothers in the first trimester and 38% to 75% at term were shown to be positive for fetal cells,[4] so the disease can occur with the first pregnancy. Apparently as little as .1 ml. of fetal cells can sensitize a woman, and approximately 5.1% of all postpartum women have .1 ml. or more fetal red blood cells.[13] If the mother does become sensitized, subsequent Rh positive babies are at risk to develop erythroblastosis fetalis.

Finn et al. in Liverpool[21] and Freda et al. in New York[20] used this knowledge to try to "neutralize" the incompatible fetal blood cells before the mother's immune system could react to them. Their initial work in Rh negative male volunteers proved that they could successfully protect an Rh negative person from becoming immunized after an injection of Rh positive blood cells by using anti-D immunoglobulins. Combined data (Tables 1 and 2) show that .6% of treated Rh negative mothers, as opposed to 7.6% of controls, became

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*Phase B Medical Student, University of Minnesota.

TABLE 1

Cumulative Data on the Prevention of Rh Immunization in Unsensitized Mothers*

	Controls		Injected	
Study	Immunized	Total	Immunized	Total
Liverpool (Finn, Clarke et al.)[21]	35	320	1	315
New York (Freda, Gorman, et al.)[22]	15	125	1	216
Long Beach (Jennings et al.)[22]	27	226	0	236
New York (Queenan et al)[22]	6	73	0	100
W. Germany (Schneider et al.)[22]	29	756	2	487
Canada (Bryant et al.)[22]	5	45	1	48
Canada (Chocon et al.)[22]	20	315	0	354
Sweden (Bartsch et al.)[22]	3	45	0	43
Edinburgh (Robertson et al.)[22]	9	101	0	87
New York (Bowe et al.)[7]	15	140	0	294
Boston (Dept. of Public Health)[1]	—	—	0	610
Leeds (Tovey et al.)[2]	—	—	29	2319
Des Moines (White et al.)[11]	1	28	0	58
Leningrad (Petrov-Maslakov et al.)[12]	8	100	0	120
Totals	173 (7.6%)	2274	33 (.6%)	5287

*Women were tested six months after delivery.

immunized after giving birth to their first Rh positive baby. During their subsequent pregnancy, 1.8% of the treated mothers as opposed to 13% of the untreated mothers became immunized. These findings are in close correlation to those of White et al.[11] (Table 3). These composite findings consider Rh negative women susceptible to immunization without regard to ABO compatibility between the mother and infant. It is known that ABO incompatibility is three times more common than Rh incompatibility,[4] and that ABO incompatibility confers partial protection against Rh hemolytic disease. If both mother and infant are ABO incompatible, the risk of sensitization (to ABO antigens) from that pregnancy is 9% to 12%. If in addition mother and infant are Rh incompatible, the risk of sensitization (to Rh antigen) only goes up to 17%.[15] Woodrow et al.[8,9] have recently studied only Rh negative and susceptible women with ABO compatibility, dividing them into "high risk" and "low risk" groups, depending on the number of fetal red blood cells found in the maternal blood stream postpartum (greater than .2 ml. constituted "high risk" while less than .2 ml. constituted "low risk." An earlier finding showed that women with greater than .2 ml. fetal red blood cells had about a 20% chance of developing immunization).[16] His findings are given in Tables 4, 5, and 6. It can be seen there is no correlation between the amount of the fetal blood loss into the maternal blood stream and the success or failure of treatment in the treated group (Dosage differences were not significant since no good study has been done to obtain the minimum effective dose).[9] This confirms a similar finding by Tovey et al.[2] They found a substantially higher number of untreated women immunized than was found in worldwide statistics i.e., 21.6% vs about 7% of primary susceptible women became immunized and 30.7% vs about 14% immunization in subsequent pregnancy. This difference can be ascribed largely to ABO incompatibility protecting the mothers from Rh immunization by clearing fetal cells from the circulation before the immune system could become stimulated. Finally, it can be seen that their earlier observation relating fetal cell blood to risk was substantiated i.e., about a 20% risk in untreated mothers with greater than .2 ml. fetal cells postpartum.

TABLE 3
Worldwide Data[23]

	1° Rh Immunization Protection		Protection in Subsequent Pregnancy	
	Immunized	Total	Immunized	Total
Treated	3 (.1%)	2880	1 (.4%)	228
Controls	84 (7%)	1200	21 (14.2%)	127

Although the exact mechanism of anti-D action is not known, various facts have come to light:

1. Essentially all treated women have no circulating fetal cells after seven days, whereas untreated women have fetal cells up to five months later.[12]
2. Sequestration in the spleen probably plays a role in clearing fetal cells. Huchet et al.[3] found a splenectomized woman with a high initial fetal blood count of 5.9/10,000, treated with two doses of anti-D postpartum did not completely clear her blood stream for five months.[3]
3. Only 4.1% of mothers form an antibody to the anti-D IgG when given the equivalent of currently recommended dosage. This anti-gamma globulin was a 19S globulin which showed no harm to mother or infant.[14]

As of June 1, 1968, *RhoGAM* was approved by the FDA. Current indications for use are:[4] (1) Mother must be definitely Rh negative; (2) Moth-

TABLE 2
Cumulative Data on the Prevention of Rh Immunization in These Same Women Following Subsequent Pregnancies.*

	Controls		Injected	
Study	Immunized	Total	Immunized	Total
Liverpool (Finn, Clarke et al.)[21]	5	43	1	40
New York (Freda, Gorman et al.)[22]	4	16	0	30
Long Beach (Jennings et al.)[22]	5	25	0	36
New York (Queenan et al.)[22]	1	1	0	2
W. Germany (Schneider et al.)[22]	10	144	0	50
St. Louis (Hamilton)[22]	16	88	0	80
Edinburgh (Robertson et al.)[22]	0	8	0	7
New York (Bowe et al.)[7]	4	16	0	42
Leeds (Tovey et al.)[2]	—	—	7	437
Des Moines (White et al.)[11]	—	—	0	9
Totals:	45 (13%)	341	8 (1.8%)	733

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*Women were tested six months after delivery.

er must not already be immunized (negative indirect Coomb's test).; (3) Baby must be definitely Rh positive; and (4) Baby must have negative direct Coomb's test. If these criteria are met, it is recommended that 250 μg of *RhoGAM* be given within 72 hours postpartum. The efficacy of this drug is such that physicians may be held legally liable if they do not give *RhoGAM* to susceptible mothers, regardless of the practice of other obstetricians in the physicians' community.[5] Current contraindications for use are:[11] (1) D patient or D^u (weak antigenic variant of D) patient; (2) Rh negative patient who has received Rh positive transfusion; (3) A patient already immunized to Rh antigen and (4) Prior to delivery.

This last contraindication is being investigated by Zipursky et al.[13] who are giving anti-D prophelactically during the last trimester. Initial results show no injury to mother or infant if given in low doses.

TABLE 4

The Prevention of Rh Immunization in Unsensitized, "High Risk" Mothers Using Anti-D Gamma Globulin.[8]

	Controls		Injected*	
Center	Immunized	Total	Immunized	Total
Liverpool	20	92	1	94
Baltimore	8	31	0	26
Sheffield	10	41	0	39
Leeds & Bradford	0	12	0	14
Totals	38 (21.6%)	176	1 (.6%)	173

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*Given 1000 μg anti-D IgG within 36 hours postpartum.

TABLE 5

The Prevention of Rh Immunization in These "High Risk" Mothers Following Subsequent Pregnancy.[8]

	Controls		Injected*	
Center	Immunized	Total	Immunized	Total
Liverpool	8	38	2	59
Baltimore	1	4	0	12
Sheffield	9	19	0	10
Leeds & Bradford	2	4	0	7
Totals	20 (30.7%)	65	2 (2.3%)	88

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*Given 1000 μg anti-D IgG within 36 hours postpartum.

TABLE 6

Study of Rh Immunization Protection Using "Low Risk" Mothers.[9]

	1° Rh Immunization Protection		Protection in Subsequent Pregnancy	
	Immunized	Total	Immunized	Total
Controls	13 (3.6%)	362	9 (10.2%)	127
Treated*	0	353	3 (2.3%)	128

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*Given 200 μg anti-D IgG within 36 hours postpartum.

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17-23. Will be found on page 55.

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(Continued on Page 64)

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Actions
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Most of the available evidence indicates that CHOLOXIN stimulates the liver to increase catabolism and excretion of cholesterol and its degradation products via the biliary route into the feces. Cholesterol synthesis is not inhibited and abnormal metabolic endproducts do not accumulate in the blood.

Indications
This is not an innocuous drug. Strict attention should be paid to the indications and contraindications.

CHOLOXIN (sodium dextrothyroxine) is an antilipidemic agent used as an adjunct to diet and other measures for the reduction of elevated serum cholesterol (low density lipoproteins) in euthyroid patients with no known evidence of organic heart disease.

The drug is also indicated in the treatment of hypothyroidism in patients with cardiac disease who cannot tolerate other types of thyroid medication.

Before prescribing, note the following: Results from a randomized clinical study have indicated a possible adverse effect when CHOLOXIN is administered to a patient receiving a digitalis preparation. There may be an additive effect. This additive effect may possibly stimulate the myocardium excessively in patients with significant myocardial impairment. CHOLOXIN dosage should not exceed 4 mg per day when the patient is receiving a digitalis preparation concomitantly. Careful monitoring of the total effect of both drugs is important.

It has not been established whether the drug-induced lowering of serum cholesterol or lipid levels has a detrimental, beneficial, or no effect on the morbidity or mortality due to atherosclerosis or coronary heart disease. Several years will be required before current investigations will yield an answer to this question.

Contraindications
The administration of CHOLOXIN (sodium dextrothyroxine) to euthyroid patients with one or more of the following conditions is contraindicated:

1. Known organic heart disease, including angina pectoris; history of myocardial infarction; cardiac arrhythmia or tachycardia, either active or in patients with demonstrated propensity for arrhythmias; rheumatic heart disease; history of congestive heart failure; and decompensated or borderline compensated cardiac status.
2. Hypertensive states (other than mild, labile systolic hypertension).
3. Advanced liver or kidney disease.
4. Pregnancy.
5. Nursing mothers.
6. History of iodism.

Warnings
CHOLOXIN (sodium dextrothyroxine) may potentiate the effects of anticoagulants on prothrombin time. Reductions of anticoagulant dosage by as much as 30% have been required in some patients. Consequently, the dosage of anticoagulants should be reduced by one-third upon initiation of CHOLOXIN therapy and the dosage subsequently readjusted on the basis of prothrombin time. The prothrombin time of patients receiving anticoagulant therapy concomitantly with CHOLOXIN therapy should be observed as frequently as necessary, but at least weekly, during the first few weeks of treatment.

In the surgical patient, it is wise to consider withdrawal of the drug two weeks prior to surgery if the use of anticoagulants during surgery is contemplated.

When CHOLOXIN is used as thyroid replacement therapy in hypothyroid patients with concomitant coronary artery disease (especially those with a history of angina pectoris or myocardial infarction) or other cardiac disease, treatment should be initiated with care. Special consideration of the dosage schedule of CHOLOXIN is required. This drug may increase the oxygen requirements of the myocardium, especially at high dosage levels. Treated subjects with coronary artery disease must be seen at frequent intervals. If aggravation of angina or increased myocardial ischemia, cardiac failure, or clinically significant arrhythmia develops during the treatment of hypothyroid patients, the dosage should be reduced or the drug discontinued.

Special consideration must be given to the dosage of other thyroid medications used concomitantly with CHOLOXIN. As with all thyroactive drugs, hypothyroid patients are more sensitive to a given dose of CHOLOXIN than euthyroid patients.

Epinephrine injection in patients with coronary artery disease may precipitate an episode of coronary insufficiency. This condition may be enhanced in patients receiving thyroid analogues. These phenomena should be kept in mind when catecholamine injections are required in sodium dextrothyroxine-treated patients with coronary artery disease.

Since the possibility of precipitating cardiac arrhythmias during surgery may be greater in patients treated with thyroid hormones, it may be wise to discontinue CHOLOXIN in euthyroid patients at least two weeks prior to an elective operation. During emergency surgery in euthyroid patients, and in surgery in hypothyroid patients in whom it may be advisable to withdraw therapy, the patients should be carefully observed.

There are reports that sodium dextrothyroxine in diabetic patients is capable of increasing blood sugar levels with a resultant increase in requirements of insulin or oral hypoglycemic agents. Special attention should be paid to parameters necessary for good control of the diabetic state in dextrothyroxine-treated subjects and to dosage requirements of insulin or other antidiabetic drugs. If sodium dextrothyroxine is later withdrawn from patients who had required an increase of insulin (or oral hypoglycemic agents) dosage during its administration, the dosage of antidiabetic drugs should be reduced and adjusted to maintain good control of the diabetic state.

When either or both impaired liver or kidney function are present, the advantages of CHOLOXIN therapy must be weighed against the possibility of deleterious results.

Usage in Women of Childbearing Age
Women of childbearing age with familial hypercholesterolemia or hyperlipemia should not be deprived of the use of this drug; it can be given to those patients exercising strict birth control procedures. Since pregnancy may occur despite the use of birth control procedures, administration of CHOLOXIN (sodium dextrothyroxine) to women of this age group should be undertaken only after weighing the possible risk to the fetus against the possible benefits to the mother. Teratogenic studies in two animal species have resulted in no abnormalities in the offspring.

Precautions
It is expected that patients on dextrothyroxine therapy will show greatly increased serum protein-bound-iodine levels. These increased serum PBI values are evidence of absorption and transport of the drug, and should NOT be interpreted as evidence of hypermetabolism; similarly, they may not be used for titrating the effective dose of CHOLOXIN (sodium dextrothyroxine). PBI values in the range of 10 to 25 mcg% in treated patients are common.

If signs or symptoms of iodism develop during CHOLOXIN therapy, the drug should be discontinued.

A few children with familial hypercholesterolemia have been treated with CHOLOXIN for periods of one year or longer with no adverse effects on growth. However, it is recommended that the drug be continued in patients in this age group only if a significant serum cholesterol-lowering effect is observed.

Adverse Reactions
The side effects attributed to dextrothyroxine therapy are, for the most part, due to increased metabolism, and may be minimized by following the recommended dosage schedule. Adverse effects are least commonly seen in euthyroid patients with no signs or symptoms of organic heart disease; the incidence of adverse effects is increased in hypothyroid patients, and is highest in those patients with organic heart disease superimposed on the hypothyroid state.

In the absence of known organic heart disease, some cardiac changes may be precipitated during sodium dextrothyroxine therapy. In addition to angina pectoris, arrhythmia consisting of extrasystoles, ectopic beats, or supraventricular tachycardia, ECG evidence of ischemic myocardial changes and increase in heart size have been observed. Myocardial infarctions, both fatal and non-fatal, have occurred, but these are not unexpected in untreated patients in the age groups studied. It is not known whether any of these infarcts were drug related.

Changes in clinical status that may be related to the metabolic action of the drug include the development of insomnia, nervousness, palpitations, tremors, loss of weight, lid lag, sweating, flushing, hyperthermia, hair loss, diuresis, and menstrual irregularities. Gastrointestinal complaints during therapy have included dyspepsia, nausea and vomiting, constipation, diarrhea, and decrease in appetite.

Other side effects reported to be associated with CHOLOXIN (sodium dextrothyroxine) therapy include the development of headache, changes in libido (increase or decrease), hoarseness, tinnitus, dizziness, peripheral edema, malaise, tiredness, visual disturbances, psychic changes, paresthesia, muscle pain, and various bizarre subjective complaints. Skin rashes, including a few which appeared to be due to iodism, and itching have been attributed to dextrothyroxine by some investigators. Gallstones have been discovered in occasional dextrothyroxine-treated patients and cholestatic jaundice has occurred in one patient, although its relationship to CHOLOXIN therapy was not established.

In several instances, the previously existing conditions of the patient appeared to continue or progress during the administration of CHOLOXIN; a worsening of peripheral vascular disease, sensorium, exophthalmos, and retinopathy have been reported.

CHOLOXIN potentiates the effects of anticoagulants, such as warfarin or Dicumarol, on prothrombin time, thus indicating a decrease in the dosage requirements of the anticoagulants. On the other hand, dosage requirements of antidiabetic drugs have been reported to be increased during dextrothyroxine therapy (see WARNINGS section).

Dosage and Administration
For **adult** euthyroid hypercholesterolemic patients, the recommended maintenance dose of CHOLOXIN (sodium dextrothyroxine) is 4 to 8 mg per day. The initial daily dose should be 1 to 2 mg to be increased in 1 to 2 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily, if that dosage level is indicated to effect the desired lowering of serum cholesterol.

When used as partial or complete substitution therapy for levothyroxine in hypothyroid patients with cardiac disease who cannot tolerate other types of thyroid medication, the initial daily dose should be 1 mg to be increased in 1 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily, preferably the lower dosage. The maximum in patients receiving digitalis therapy is 4 mg.

For **pediatric** hypercholesterolemic patients, the recommended maintenance dose of CHOLOXIN is approximately 0.1 mg per kilogram. The initial daily dosage should be approximately 0.05 mg per kilogram to be increased in up to 0.05 mg per kilogram increments at monthly intervals. The recommended maximal dose is 4 mg daily, if that dosage is indicated to effect the desired lowering of serum cholesterol.

If new signs or symptoms of cardiac disease develop during the treatment period, the drug should be withdrawn.

How Supplied
CHOLOXIN (sodium dextrothyroxine) is supplied in prescription packages of scored 1, 2, 4, and 6 mg tablets.

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Review

Lymphocytes and the Immune Response*

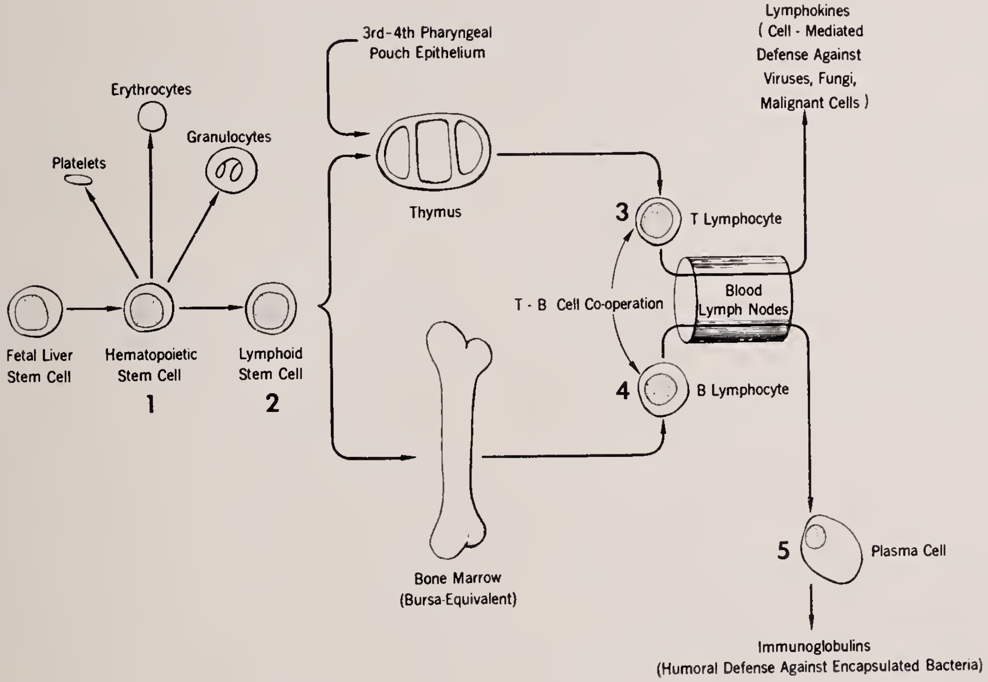
JOHN H. KERSEY, M.D.†

Clinical defects have been described in the pathway of development of lymphocytes from the hematopoietic stem cell to fully developed T and B lymphocytes. Defects early in differentiation tend to be more severe and present at an earlier age. Clinically, one should suspect primary immunodeficiency in any individual with severe repeated infections, severe eczema unexplained arthritis or deficiencies of red cells or platelets. Using the current therapeutic armamentarium many of these individuals can be expected to lead normal lives when treated with proper antibiotics, plasma and gamma globulin therapy and in more severe cases, bone marrow or leukocyte extracts.

KNOWLEDGE OF THE essential role of lymphocytes in the immune response has significantly expanded in the past few years. Lymphocytes are responsible for immunologic memory and are essential in host defenses against bacteria, fungi, viruses and malignant cells. Understanding the role of lymphocytes has been aided by study of patients with immunodeficiency diseases that have abnormalities of one or more lymphoid cell types. As illustrated in the accompanying figure, several forms of lymphocytes are now known.[1]

Lymphocytes which have come under the influence of the thymus are known as T cells or thymus-derived cells. These cells begin differentiation (maturation) within the thymus and fully differentiate in the peripheral lymphoid tissue, largely in lymph nodes and spleen. These lymphocytes are largely responsible for cell-mediated immune defense against viruses, fungi and malignant

LYMPHOCYTE DIFFERENTIATION


3rd-4th Pharyngeal Pouch Epithelium
Lymphokines (Cell - Mediated Defense Against Viruses, Fungi, Malignant Cells)
Erythrocytes
Granulocytes
Platelets
Thymus
3
T Lymphocyte
T - B Cell Co-operation
Blood Lymph Nodes
Fetal Liver Stem Cell
Hematopoietic Stem Cell
1
Lymphoid Stem Cell
2
4
B Lymphocyte
5
Plasma Cell
Bone Marrow (Bursa-Equivalent)
Immunoglobulins (Humoral Defense Against Encapsulated Bacteria)

Figure—Steps in differentiation of lymphocytes from stem cell precursors to fully immunocompetent T and B lymphocytes.

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*Presented at the Annual Meeting of the Minnesota State Medical Association in Minneapolis, May 24, 1973.

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cells. They do not produce significant amounts of antibody but operate directly to kill foreign invaders through soluble products known as lymphokines.

As illustrated in the accompanying figure, the other source of cells in the lymphoid system is the B cells, which derive their name from their origin in bone marrow or, in the chicken in a lymphoid organ known as the bursa of Fabricius. B cells are characterized by surface immunoglobulins and have the capacity to fully differentiate into immunoglobulin-secreting (plasma) cells. Effects of the B cell system are largely mediated through antibody (immunoglobulin) which is responsible for the defense against encapsulated bacterial organisms such as meningococcus, hemophilus influenza, and pseudomonas aeruginosa.

Immunodeficiency Diseases from Lymphocyte Abnormalities

The cell represented as #1 in the Figure is a hematopoietic stem cell. Platelets, red cells, granulocytes and lymphoid cells develop from this cell. A rare genetically determined disorder in which children apparently lack this stem cell is characterized by deficient platelets, red cells, granulocytes and lymphoid cells; they subsequently die of bleeding or overwhelming infection. The cell which differentiates into T of B lymphocytes is known as the lymphoid stem cell and is shown as #2 in Figure. Stem cells appear to be abnormal in patients with immunodeficiency syndromes characterized by deficiencies of both cell-mediated (T) and humoral (B) immunity.[2]

Abnormalities of T and B cell systems are generally genetically determined, usually autosomal recessive, and frequently affect more than one child in the family. This combined system immunodeficiency syndrome should be suspected when a child develops multiple severe infections, especially pneumonias, during the first few months of life. Cell-mediated immune responses, including delayed hypersensitivity skin tests, lymphocyte responses and quantitative immunoglobulins are depressed. When untreated these children usually die within the first year or two of life, generally with severe infections or sometimes with cancer. Current therapy includes fresh frozen plasma, preferably from a parent, as a source of immunoglobulins, lymphocyte transfer factor as a source of information molecules for lymphoid cells or bone marrow transplant as a source of immunocompetent lymphoid cells.

Lymphoid stem cells are also abnormal in ataxia-telangiectasia, delayed onset (variable) immunodeficiency and Wiskott-Aldrich syndrome. Ataxia-telangiectasia presents in childhood with severe infections and unsteady gait due to cerebellar dysfunction. Telangiectasia usually develops later. The children die of severe infections or, less frequently, cancer. Late onset (variable) immunodeficiency develops most generally after the age of 50 and results in frequent infections, but is also associated with a high risk of development of lymphoid and epithelial malignancy. Children with Wiskott-Aldrich syndrome have abnormalities of humoral and cell-mediated immunity, low platelets and severe eczema. This syndrome is usually fatal, due to severe infections or bleeding into the central nervous system.

An isolated abnormality of T (thymus-derived) lymphocytes (#3 in Figure) is present as part of an embryologic defect of the 3rd and 4th pharyngeal pouch (Di George syndrome), in which parathyroids are also absent. These children develop tetany and severe infections; untreated children generally die during the first several months of life. The immunologic defect is generally correctable with a thymic transplant.

Absence of B lymphocytes (#4 in Figure) is found in the genetically determined disorder of childhood known as sex-linked (Bruton's) agammaglobulinemia. Lack of B lymphocytes in these individuals results in absence of plasma cells and immunoglobulins. Cell-mediated immunity remains intact. Patients with this disorder are infant boys who present with bacterial infections, usually caused by encapsulated organisms. These patients can generally be satisfactorily treated with plasma or gamma globulin.

Immunodeficiency Diseases from Plasma Cell Abnormalities

The final differentiation of B lymphocytes is into plasma cells, the cells which are responsible for production of antibody of all classes. Some individuals have intact B lymphocytes but absence of plasma cells and immunoglobulins (#5 in Figure) resulting in another form of agammaglobulinemia. This condition is also associated with frequent infections, which are usually bacterial in nature. Cell-mediated immunity remains intact in these individuals, and they are unlikely to have difficulty with viral or fungal infections.

This condition, which usually presents in childhood, can be well controlled with gamma globulin and plasma therapy.

Neoplasia Results from Uncontrolled Proliferation of Lymphoid Cells

Lymphoid malignancies are the result of uncontrolled proliferation of lymphoid cells. Chronic lymphatic leukemia, for example, is usually the result of uncontrolled proliferation of immunoglobulin-bearing B lymphocytes.[3] Similarly, Burkitt's lymphoma of both African[4] and non-African origin[5] often involves B lymphocytes. Acute lymphoblastic leukemia, on the other hand, sometimes involves T lymphocytes.[6] Some cases of acute and chronic lymphoid leukemias, appear to involve neither T nor B lymphocytes and may originate from undifferentiated or stem cells.

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Laboratory Letter

Creatine Phosphokinase (CPK) as Part of a Screening Profile: A One Year Survey

"If we begin with certainties, we shall end in doubts; but if we begin with doubts, and are patient in them, we shall end in certainties."—Sir Francis Bacon, De Augmentis

Many laboratories are introducing Creatine Phosphokinase (CPK) as part of multiphasic profiles. But what does an abnormal CPK usually mean as part of a screening chemical profile? That was one question that faced our laboratory when we began to send out profiles containing CPK results a year ago.

We were uncertain about what the CPK might mean. Not that we didn't try. We read the CPK literature, but that didn't help much. After all, what one reads and what one sees may differ, particularly when the reading involves preselected studies of specific diseases and the screening applies to monitoring, evaluating, and screening of many diseases.

Hedging Doubts

To hedge our doubts, we began a tracer study of CPK elevations. When an SMA—6 or SMA—18 yielded a high CPK, we would occasionally send a self-return postcard with the high CPK report.

Using this simple method, we've traced some of the causes for high CPK for 211 patients (see Table). We shall now discuss some of these causes.

TABLE
Results of CPK Survey in 211 patients in whom CPK was elevated in SMA-6 and SMA-18 Profile (Normal upper limit for CPK is 150 Units/ml).

Problem	Number of Patients	Highest Value (Units/ML)	Mean Value (Units/ML)
Hypertension	35	923	276
Muscle spasm, cramps, or musculoskeletal pain, low back spasm	25	298	205
Miscellaneous conditions not known to be associated with CPK elevations	22	308	191
Muscle disease (myositis, dystrophy)	21	4330	1166
IM injections	19	562	301
Myocardial infarction	15	2730	930
Hypothyroidism	13	2883	926
Trauma with muscle injury	12	452	296
Pancreatitis	12	507	452
Strenuous exercise	10	512	447
Alcoholism	10	508	297
Stroke or other acute brain damage	9	259	225
Necrosis (gangrene, radiation damage)	5	275	226
Recent surgery	1	228	228
Choloxin therapy	1	283	283
Mononucleosis	1	610	610

Results of Survey

Do the results of this survey surprise us?

Well, no and yes.

No

For example, we expected the following conditions (muscle disease, myocardial infarction, and hypothyroidism) to have the highest average CPK levels and they did.

	CPK Values		
	Highest	Mean	Average Increase of Upper Limit
Muscle Disease	4330	1166	8 fold increase
Myocardial Infarct	2730	930	6 fold increase
Hypothyroidism	2883	926	6 fold increase

These levels are in keeping with observations in the recent literature, and therefore confirm what we anticipated.

We weren't surprised by elevations in other conditions that we had come across in our literature search. These included some of the following problems:

	CPK Values		
	Highest	Mean	Average Increase of Upper Limit
IM Injections	562	301	2 fold increase
Trauma	452	296	2 fold increase
Strenuous Exercise e.g. jogging	512	447	3 fold increase
Stroke or brain damage	259	225	1½ fold increase
Alcoholism	508	297	2 fold increase
Necrosis, recent surgery	275	225	1½ fold increase

These results, fell in the ballpark, but are worth a few stray notes. In one healthy 45-year-old jogger we picked up a CPK of 512 units. At the time of the CPK elevation, he was out of condition, and had just started his vigorous exercise program. Later CPKs, when he was in condition, were normal. This fits with the literature: unfit men have high CPKs after strenuous exercise; fit men usually don't.[4-6]

For your information, you may want to know the drugs that have been reported to cause high CPKs. These include:

Drug	Reference	Drug	Reference
Amphotericin B	7	Electrocautery	14
Amphicillin	8	Ethanol	15
Analgesics	9	Ethchlorvnyl	10
Barbiturates	10	IM Injections	13
Carbenicillin	8	Insulin	16
Carbromal	10	Morphine	9
Clofibrate	11	Penicillin	17
Clonidine	12	Phenothiazines	18
Digoxin	13	Succinylcholine	19
Diuretics	9	Tubocurarine	9

Yes

But some of the survey results did surprise us.

For example, that ten percent (22 of 211) of the patients had nothing other than nonspecific muscle pains and aches was unexpected. In our minds we don't associate such aches and pains with muscle damage. Yet it's been reported such weekend activities as a brisk two-hour walk or two days of intense physical labor can elevate the CPK.[20] So can influenza: in 14 of 21 children with flu, CPKs were up during the acute phase of the illness.[21]

Hypertension

What surprised us the most was that nearly 17 percent (35 of 211) patients had hypertension. In thirty of these patients, physicians reported that the patients were on diuretics. We first guessed that diuretic-induced hypokalemia might be the problem. Why? Because hypokalemia with myopathy has been often reported to produce high CPK's.[22] But the evidence was not completely convincing. Twelve of the 35 (or 34 percent) had hypokalemia. Perhaps the high incidence of hypertension in our survey resulted from a biased sampling. After all, many physicians order the multiphasic profiles to monitor diuretic therapy, and diuretics are often prescribed for hypertension.

Pancreatitis

Lastly we were a little surprised that 12 of our 211 patients had pancreatitis. In eight patients, acute pancreatitis was their primary problem; in three, the pancreatitis was secondary to a penetrating duodenal ulcer; and in one patient, the pancreatitis was secondary to steering wheel injury. That an inflammed pancreas should lead to an elevated CPK probably should be anticipated. Pancreatic juice is highly toxic stuff, and once loose in the retroperitoneal space, it has ready access to the psoas muscles. Other authors, incidently, have reported high CPKs in pancreatitis.[23]

Conclusion

We should like to close with this observation about our 211 patients with high CPKs: besides expected elevations in conditions that affect muscle or brain tissue, CPK may be elevated in lesser degrees with nonspecific muscle aches, cramps, and spasms; with strenuous muscular exercise; with hypertensive persons being treated with diuretics; and with acute pancreatitis. About ten percent of the time, we could not explain CPK elevations. In the main, we concluded CPK is a useful addition to screening profiles, although occasionally one has to search patiently for the cause of abnormal CPK results.

Richard L. Reece, M.D.
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Age in a virtuous person, of either sex, carries in it an authority which makes it preferable to all the pleasures of youth*

---

*Sir Richard Steele, The Spectator #153, August 25, 1711.

Excerpts From A Presentation by Senator Nicholas Coleman

SENATOR NICHOLAS COLEMAN*

"HEALTH CARE is a right and not a privilege" was the phrase which most affected health care legislation during the first half of the 68th Minnesota Legislature. In dealing with health care problems we found that high cost and inadequate delivery systems most often precluded the fulfillment of that adage.

"Before talking to you about specific health care issues Id' like to give you some idea of what we're going to be doing at the Capitol in the way of research. Rep. Berg has already talked to you about the extra staffers being provided to the health committee through the Citizen's Conference on State Government grant from the Robert Wood Johnson Foundation. This is going to be quite important because it has gone beyond just somebody dabbling in the health area. It has gotten to the point where a number of people are going to have professional answers for health care questions facing the people of Minnesota.

"When I went to the Minnesota Senate eleven years ago there were no research people outside of an ineffective joint research facility. There are now seventeen professional people in Senate Research, our non-partisan research operation. In addition, each caucus alone is authorized seven research people. Recently, the Senate and House of Representatives jointly named a Director to coordinate legislative research activities, and I have been pressing him to hire additional personnel. Our caucus has actually authorized me to obtain a hundred research people. Well, I frankly don't know right now what we would do with a hundred professional research people but I'm sure that like any other bureaucracy we will eventually find out and be able to build our research facilities to where a hundred is inadequate.

"Some of the information on health costs which our researchers have turned up recently is quite interesting. The fact that health care is becoming exceedingly expensive makes it a privilege of the rich who can afford to be sick. In 1960, the average cost of a hospital room was $32 a day. Today that cost is $91—a 285% increase. Your own salaries have also gone up—about 100% in this same period. Hospital costs have obviously risen faster, but in the mind of the public you are all in this together.

"The information we have states that in Minnesota physicians in group practice have a mean income of $118,000 a year; physicians in partnerships, $69,000 a year; and those in solo practice, $49,000 a year. Now this is the information furnished to our Health Subcommittee by somebody. If that is incorrect, and I see a few startled expressions around . . . you doctors in solo practice are going to quit this afternoon and join a group someplace. However, these are the figures that are available to our committee. We'll be looking at them a little more, but if they are not accurate then we should know about it because this is the kind of information on which we are basing conclusions.

"The prices charged for medicine have also jumped rapidly. One Twin Cities hospital administers aspirin for 75¢ each while retail aspirin prices are approximately 29¢ per 100—a possible 25,860% markup.

"Government is directly related to the problems of health care when we look at medical assistance and welfare payments. These totaled $121 million in 1972. They have risen to $189 million in 1973. Now that's a significant jump. It is unlikely that costs will continue to increase at this rate because of decreased rate of population growth, but it may be that we will simply shift the expenditures from the children to the elderly. Maybe we're not going to change the total welfare costs but simply move them around.

"I recently had a press conference which was not greeted with universal acclaim by the medical profession saying that welfare units would have to adopt standards of payment and enforce them.

---

*Senator Coleman is the present majority leader of the Minnesota Senate. His presentation from which this article developed was given at a meeting of the Minnesota State Medical Association Committee on Public Policy and Legislative Contact Physicians on October 20, 1973 at the Radisson South Hotel.

Only Ramsey County was doing it and we thought they should be enforced on a universal basis. I was quite clear in the press release that I was not charging chicanery on the part of the profession but I was also certain of the information that we had that the citizens of the state of Minnesota—and you are in that group too—are paying at least a million dollars more than they should for medical assistance on the basis of inadequate audit of welfare costs. This doesn't make sense. It penalizes the careful practitioner and forces costs to go up everywhere else. We will all be better off when there is a very strict accounting for what is spent in the area of medical payments. The new system of computerized central payments for public assistance medical aid authorized by this legislature will accomplish this. It will speed payments and permit monitoring of costs under a fee schedule for physicians and hospitals which will be standardized statewide.

"Problems of health care, however, go far beyond spiraling costs. For example, urban areas receive substantially better care than rural areas. While nearly one-third of the population lives in the rural areas, only 12% of the nation's physicians live there. This is a national average but the state of Minnesota is not significantly different. There are a number of reasons for this imbalance; what can we do to make some changes in this distributive pattern?

"Another area needing attention is preventive medicine. There has been a lot of talk about it for years but we haven't done much in the state legislature to encourage it. We want to find out why we can't get health care before we become seriously ill. Obviously cost is a factor, but what can be done about it? We would like to have physicians and hospitals practicing independently and fighting for business in an area. Talk of fighting for business may sound strange to the medical profession but there are those who think the cost of medical care won't really come down until Dr. Brown starts whispering that he does an appendectomy cheaper because he does it faster and because he doesn't have the standard of living that Dr. X maintains. This kind of competition would be good to a certain extent. We're going to look at possible solutions to the continuing problems of equitable health care services and we're going to look at a system which would stress preventive care, would provide adequate coverage in all geographic areas, is competitive, is reasonably priced, and provides for rapid disbursement of government assistance funding. We are going to go ahead and do it. We would like to do it with your cooperation because you are a respected part of your community and you do have the facts and figures. But we can't pretend that there's not going to be anything happening anymore. It used to be that we had a 120-day straight session all in one biennium and we had no staff. We would go away for 18 months and not bother particular sections of the community and you would assume that nothing would be done. This is not true anymore. It is going to be done and it means changes in the way the state encourages the delivery of health care. We would like you to participate in seeing that it is done.

"HMO's are one thing that we have already tried. I would have been more crushed to have lost my HMO bill in 1971 than in the '73 session because I'm not now sure whether HMO's are the answer. We'll be working in the area of catastrophic health insurance, health care manpower incentives, and reducing the cost of health care delivery. We are putting additional money into programs designed to encourage an increase in the number of physicians in outstate practice. Forty-five additional positions at the University Hospitals have been funded. Family practice residency programs received 2.7 million dollars for the biennium. This legislature authorized a special loan program for medical students who agree to practice in rural areas. A student can receive up to $6,000 a year at 8% interest that is completely forgiven if he practices in a rural area for three years. We gave 10.7 million in funding for the state's 27 community mental health centers, 3.2 million for group homes for the mentally retarded, 1.3 million for planning in programs for emotionally disturbed children, and 3.6 million for day activity centers, just to mention a few of the programs we undertook this past session.

"Much is yet to be done in the area of health care and, as a profession, you can be most helpful in our future study and legislative action. Is health care insurance adequate? What special type of health care problems face us now? What can we expect in the future? What are the most effective preventive medicine techniques? What type of incentive will convince medical professionals to practice outstate? How can we reduce costs and increase service?

"We should be looking into the area of malpractice suits. I don't know why the HMO Act prohibits arbitration for malpractice suits but we should look at it and perhaps change it. I don't find it at all amusing to see a claim settled for three quarters of a million dollars such as was publicized recently because it merely sends up your insurance coverage costs which in turn reflect themselves in increased costs to your patients.

"We would also like to encourage you in some way to find a better method of policing your profession. I'm not satisfied that it is being done correctly. There has to be some system other than simply suspending a man's license, such as fines or other types of reprimand short of revocation of license.

"In the area of health manpower incentives, we're going to be talking more about allied health care personnel. You and I have had a difference of opinion on this for several years. This is one that I keep losing all the time, but I'm mean, and I'm persistent, and we're going to get back to it again in 1974 and 1975 and 1976. I don't believe it's realistic for you to expect to get just a delegatory statute that allows you, in effect, to be your own medical school. You should be able to delegate more, but I think it has to go in line with training programs in health care services.

"As you can see, the legislature is ready to tackle a number of health care problems, however, our solutions cannot be assured of success without the input of health care professionals such as yourselves. I would ask you to contemplate the areas I have outlined for you, whether as an organization or as individuals, and help us gather the information we need to appropriately respond to Minnesota health care problems and needs. We very much need and want your help. Thank you very much."

Senator Coleman, in looking ahead in the area of health care legislation, points out the critical need for more physician involvement in the legislative process. Non-physicians are and will be playing an increasing role in planning and legislating medical decisions in future legislative sessions. Hopefully this article will stimulate more MSMA members to become interested and active in legislative matters. Medicine MUST participate in the formulation and shaping of decisions relating to health and medical care or we shall soon be mastered by those who do.

C. A. Anderson, M.D., Chairman
Committee on Public Policy

121st Annual Meeting of State Association Scientific Program Team Assembled

The members of the Scientific Assembly Committee, under the chairmanship of *Robert D. Semsch, M.D.*, are: *Martin A. Adson, M.D.; Robert F. Avant, M.D.; Paul F. Bowlin, M.D.; Richard A. Chilgren, M.D.; Gerald A. Close, M.D.; William E. Jacott, M.D.; John G. Mayne, M.D.; Harley J. Racer, M.D.; Donald VanRyzin, M.D.* Ex-officio members include: *Barnard Hall, M.D.; George B. Martin, M.D.; Robert L. Powers, M.D.; John J. Regan, M.D.; Mr. Harold W. Brunn. Douglas Fenderson, Ph.D.*, Director of the Continuing Medical Education Department of the University of Minnesota has been invited to attend as a special guest, to advise on program planning presentation.

Classified Advertisements (continued)

(Continued from Page 50)

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Symposium on Renal Disease

Sponsored by: Minnesota Society of Clinical Pathologists

Date: Saturday, March 30, 1974

Place: Marquette Inn, Minneapolis

10:00-11:00 a.m.: Urinalysis as it relates to renal function.
David Wilson, M.D. and Mary Bradley, M.D.

11:00-12:00 noon: Classification of renal pathology as determined by light microscopy.
Abe Fox, M.D.

12:00- 1:30 p.m.: Luncheon

1:30- 2:30 p.m.: Acute renal failure.
John Crosson, M.D. and Donald Duncan, M.D.

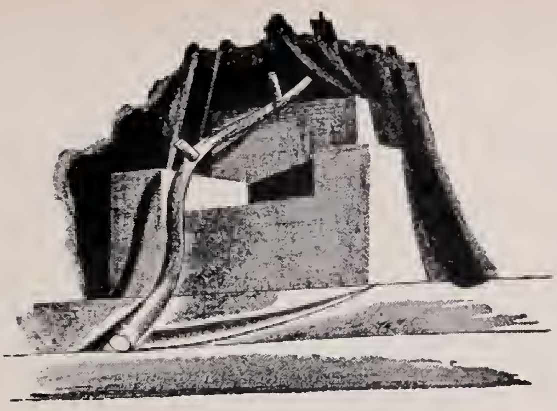
2.30- 3:30 p.m.: Childhood nephrosis.
Barbara Burke, M.D., Robert Vernier, M.D. and Alfred Michael, M.D.

4:00- 5:00 p.m.: Lupus nephritis.
Keith Holley, M.D. and James Donadio, M.D.

Tuition: $5.00 (includes lecture summaries and booklet of 35 mm. slides)

Luncheon: $5.00

Applications: Before March 15 to: Seymour Handler, M.D., Secretary, Minnesota Society of Clinical Pathologists, 3220 Lowry Avenue, North, Minneapolis, Minneosta 55422.



In Memoriam

SUMNER S. COHEN, M.D.

Dr. Sumner S. Cohen, 71, retired medical director of Glen Lake Sanatorium, died December 10. A specialist n the field of tuberculosis and respiratory diseases, Dr. Cohen also had been a consultant to the U.S. Public Health Service and the Veterans Administration Hospital. A native of Boston and a graduate of the University of Minnesota Medical School, Dr. Cohen had been also in private practice since 1957.

He was a past president of the Minnesota Rehabilitation Association, regional president of the National Rehabilitation Association and president of the Minnesota Trudeau Association. In addition, he was a member of the American Medical Association and the Hennepin County Medical Society and a Life Member of the Minnesota State Medical Association.

Dr. Cohen is survived by his wife, Dora, and a son, Edward.

NATHANIEL H. LUFKIN, M.D.

Dr. Nathaniel H. Lufkin, 75, Minneapolis pathologist, died December 6. He was a graduate from Carlton College of Northfield, and the University of Minnesota Medical School.

Dr. Lufkin was an associate professor at the University of Minnesota and a staff pathologist at Hennepin County General Hospital, St. Barnabas and Veterans Hospitals. He founded Lufkin Medical Laboratories of Minneapolis in 1953.

A former president of the Minnesota Pathological Society and the Minnesota Society of Clinical Pathologists, Dr. Lufkin was a member of the American Medical Association and the Hennepin County Medical Society and an Associate Member of the Minnesota State Medical Association.

He is survived by his wife, Florence, a daughter, Mrs. Lee Hardisty, and two sons, Dr. C. Dexter Lufkin of Hawaii and Dr. Murray Lufkin of St. Paul.

WALLACE H. COLE, M.D.

Dr. Wallace H. Cole, 85, St. Paul orthopedic surgeon, died November 12. Dr. Cole had joined the staff of Gillette State Hospital for Crippled Children in 1912 and for many years was the head of the surgery department at the Shrine Hospital for Crippled Children in Minneapolis.

He was a graduate of the University of Minnesota Medical School and a member of the American Medical Association, the Ramsey County Medical Society and the Minnesota State Medical Association.

Dr. Cole is survived by two sons, F. Crunden and Wallace.

JAMES F. ZAGARIA, M.D.

Dr. James F. Zagaria, 60, St. Paul anesthesiologist, died November 15. He was a graduate of the University of Minnesota Medical School.

Dr. Zagaria was a member of the Minnesota Society of Anesthesiologists, American Medical Association, American Society of Anesthesiologists, Minnesota State Medical Association and the Ramsey County Medical Society.

He is survived by his wife, Marie, and sons, James F. Jr., Mark C. and Paul A.

NATHANIEL J. BERKWITZ, M.D.

Dr. Nathaniel J. Berkwitz, 74, Minneapolis psychiatrist, died November 13. He graduated from the University of Minnesota Medical School.

A former instructor of the University of Minnesota, former consultant of the Glen Lake Sanatorium, and former staff member of Hennepin County General Hospital, Dr. Berkwitz was a member of the American Medical Association and the Hennepin County Medical Society and a Life Member of the Minnesota State Medical Association.

He is survived by his wife, Josephine, daughter, Mrs. Robert Stender and son, Robert.

JOHN W. AUGHENBAUGH, M.D.

Dr. John W. Aughenbaugh, 45, Minneapolis obstetrician, died November 27. He was a member of the American Medical Association, Minnesota State Medical Association and the Hennepin County Medical Society and a graduate of the University of Minnesota.

HUGH OWEN MORGAN, M.D.

Dr. Hugh O. Morgan, 64, Amboy physician, died October 22. He had practiced in Amboy since 1936.

A member of the Minnesota State Medical Association, the American Medical Association and the Blue Earth County Medical Society, Dr. Morgan had also been the health officer for Amboy.

He is survived by his wife, Lilly, a son, Owen H., and a daughter, Mrs. Gary Bachmann.

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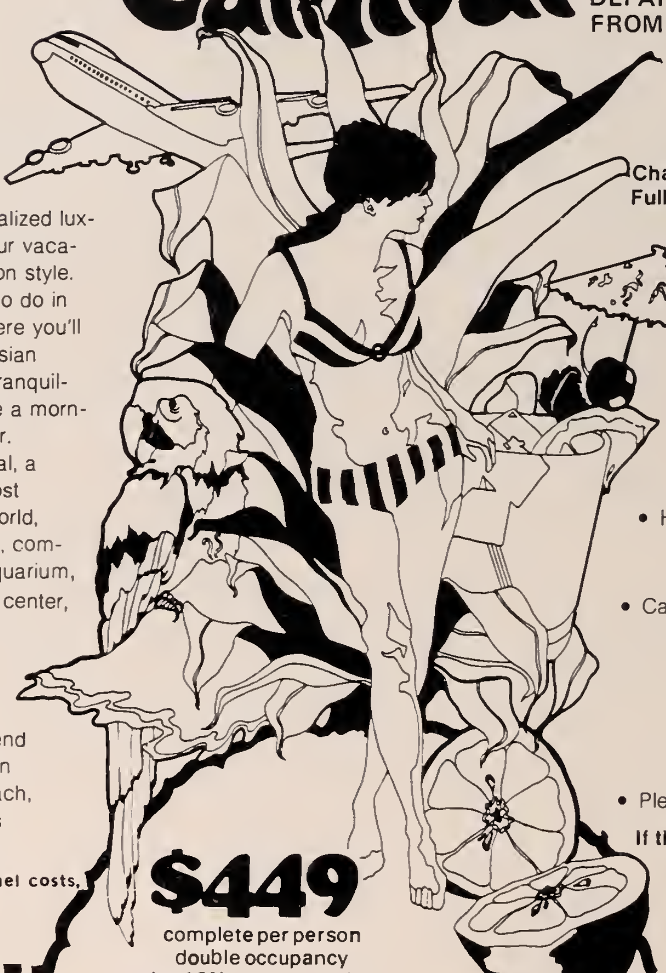

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Book Reviews

SYNOPTIC FUNCTIONAL NEUROANATOMY. Wendell J. S. Krieg, Ph.D. Brain Books, Evanston, 1973. 74 pages.

Who does not look back with tremulousness upon the hours spent in acquiring the rudiments of neuroanatomy in medical school? Beads of perspiration may still be brought forth upon the forehead at the mere thought. Only a very few of those fledgling physicians ever need to utilize detailed neuroanatomy in their later practice. Yet, in diagnosing neurological disease, it is absolutely essential to know neuroanatomy—the more, the better. No physician can be ignorant of the main plan of neuroanatomical organization and do justice to his patients because neurological disorders constitute a significant proportion of the problems encountered even by the family practitioner.

A simple, no nonsense, plain English review of neuroanatomy with handy pictures, preferably color coded, is what is needed and that is exactly what Krieg attempts to provide in his *Synoptic Functional Neuroanatomy*. He offers the synopsis at three levels—the first (Text I) is an overview to medical students; the second level (Text II) is addressed to the medical students and, in part, to dental students and speech therapists; the third level is for those with good background who desire a "quick refresher." The first text is six and a quarter pages in length, the second is 53 pages long and the quick refresher outline is over in but four painless pages.

Impossible as its seems at first inspection, a serious attempt to use Krieg's synopsis will, I believe, succeed in accomplishing Krieg's goal. In any event, at $5.00 (or $6.00 for a hard-bound version), the student's financial investment is small even if he finds that the book falls short of his needs.

Milton Alter, M.D., Ph.D.
Chief, Neurology Service
Minneapolis VA Hospital

A SYNOPSIS OF CONTEMPORARY PSYCHIATRY —George A. Ulett, M.D., C. V. Mosby Co., $10.90. 367 pages.

This volume now in its fifth edition is reviewed for the first time in MINNESOTA MEDICINE. Within the limitations imposed on a text such as this, it is comprehensive in its coverage. While of necessity brief, it is well written, factual, clear in presentation and very readable. Of the three sections: (1) History Taking and Diagnostic Procedures, (2) Clinical Syndromes and (3) Therapeutic Measures, the latter is exceptionally well presented. One added feature is the large number of listed references.

For the beginning student, the busy practitioner and for quick reference this volume is recommended.

Reynold A. Jensen, M.D.
Minneapolis, Minnesota

SURGICAL DIAGNOSIS & TREATMENT. J. Englebert Dunphy, M.D. and Lawrence W. Way, M.D. Lange Medical Publication, Los Altos, California. 1973. 1108 pages.

This is a well-bound paperback compendium of the very extensive field of "Surgical Diagnosis & Treatment." It deals with the essential and most recent material in the field of Surgery. It comprises fifty-two chapters written by men who are well qualified to review their field of interest.

Most of the illustrations are line drawings upon which the Ben Day effect has been used to advantage with the application of Zip-A-Tone.

No one surgeon can encompass the entire field of surgical knowledge, but because most surgeons have a wide interest, it is comforting to have a source from which he can readily obtain the basics in many of his secondary fields of interest.

This book in that regard serves as an excellent source of reference of the most current problems in surgical diagnosis and treatment.

Carl O. Rice, M.D., Ph.D.
Editor Emeritus

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Pediatric Day

Pediatric Day will be held March 16 at the Mayo Clinic. The program will be comprised of a series of talks by the Department of Pediatrics of the Mayo Clinic and Mayo Medical School relating to problems in pediatric practice.

Dr. John D. Nelson, Professor of Pediatrics at the University of Texas, will be the guest speaker and will speak on subjects relating to pediatrics and infectious disease.

Write: Dr. E. C. Burke, Professor of Pediatrics, Program Director, Mayo Clinic, Rochester, Minnesota, 55901 for information.

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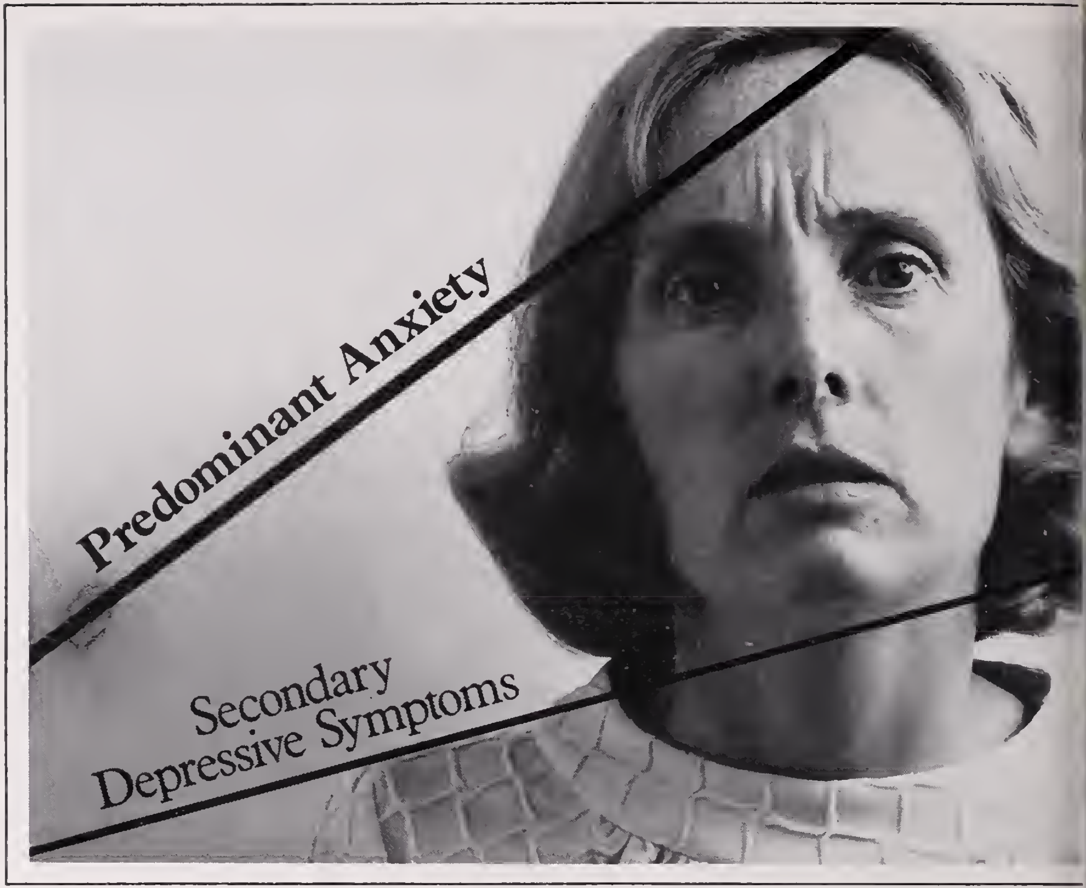
vol. 57 #



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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant
medication; abrupt withdrawal
be associated with temporary increase in frequency and/or sever
of seizures. Advise against simul
taneous ingestion of alcohol and
other CNS depressants. Withdra
symptoms (similar to those with
barbiturates and alcohol) have
occurred following abrupt disco
tinuance (convulsions, tremor, a
dominal and muscle cramps, vomi
and sweating). Keep addiction-p
individuals under careful surveil
lance because of their predisposi
to habituation and dependence. I
pregnancy, lactation or women o
childbearing age, weigh potential
benefit against possible hazard.

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Frequently, the patient's symptoms are greatly intensified at bedtime. In such situations, Valium offers an additional advantage: adding an *h.s.* dose to the *b.i.d.* or *t.i.d.* schedule can relieve the anxiety and thus may encourage a more restful night's sleep.

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Precautions: If combined with psychotropics or anticonvul- , consider carefully pharma- y of agents employed; drugs as phenothiazines, narcotics, turates, MAO inhibitors and antidepressants may poten- its action. Usual precautions ated in patients severely de- ed, or with latent depression, th suicidal tendencies. Observe precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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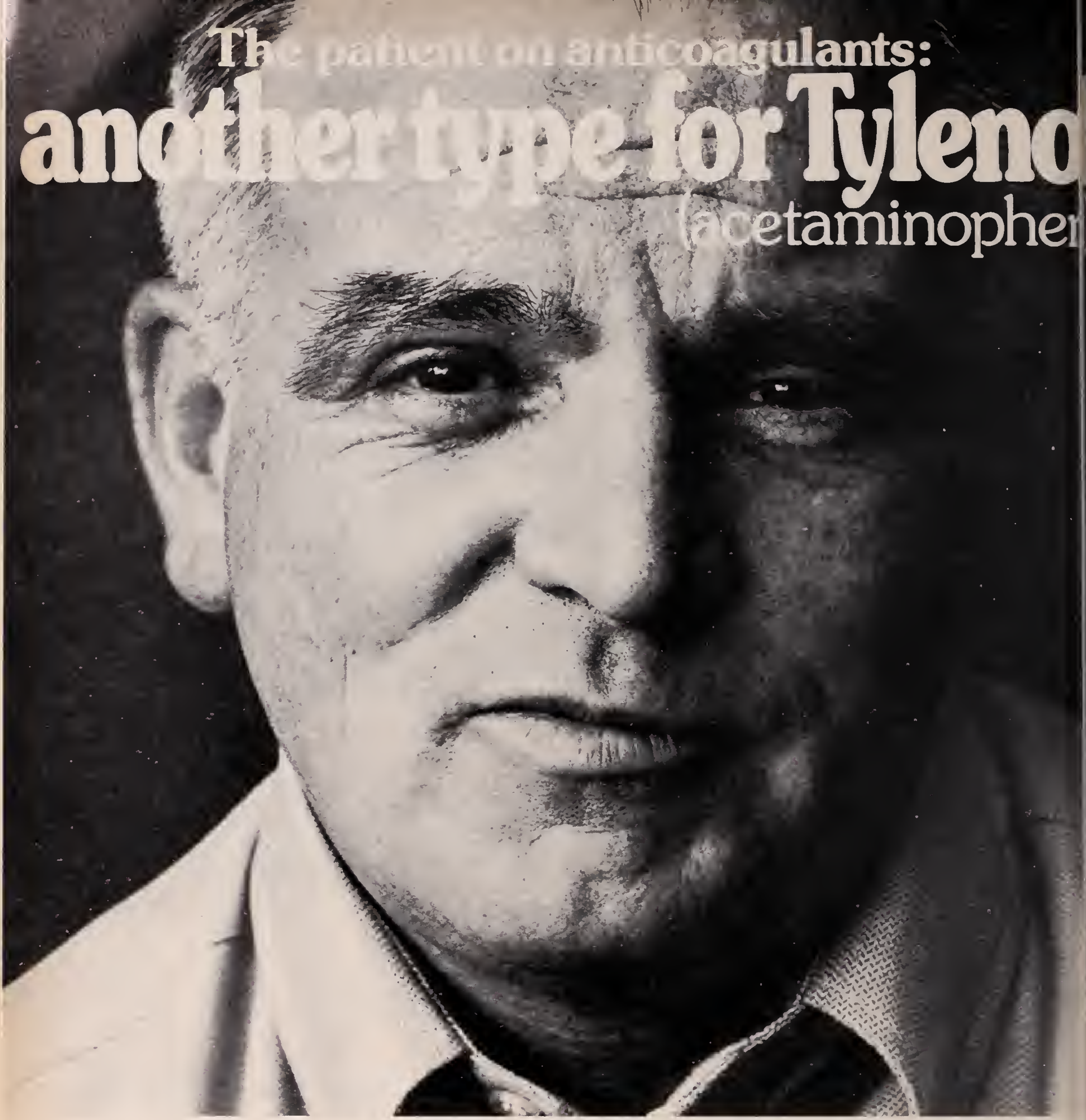

When the patient on anticoagulant therapy has a condition requiring an analgesic, a new problem arises. Aspirin frequently causes prolonged bleeding time and occult gastrointestinal bleeding.[1-3]

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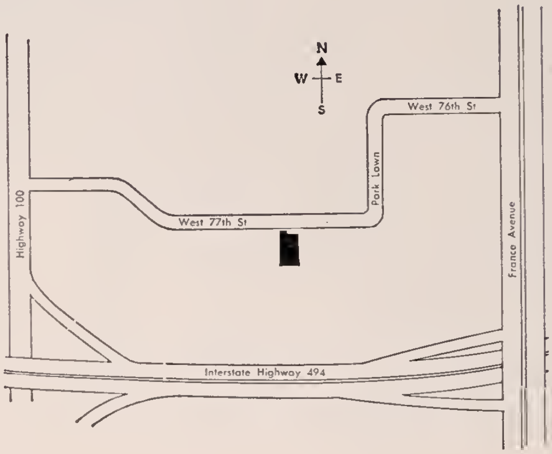

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President's Letter

AMA Meetings

My wife and I are sitting peacefully in the club car of Santa Fe's Super Chief (still a great train) as it pounds across the incredibly lovely desert of northern New Mexico on our leisurely return from AMA Clinical 73. This great confluence of physicians, one of two the AMA sponsors each year, is multifaceted—academic, social, industrial, political and consequently peripatetic. The clinical section, as always, is excellent, bringing much that is new to the attention of our colleagues while concurrently restating many of the old basic principles. Our own Harry Hall with his fracture demonstration is a perennial contributor to the clinical section as is Dick Steinhilber of the psychiatric section.

The industrial segment of AMA meetings, indeed of most medical meetings, is a peculiar blend of science and hucksterism, of dignity and marketplace, of dollars and compassion. It is an inescapable and in many ways valuable adjunct to most medical conventions.

The social aspects of AMA meetings is something else! There is much hilarity in corridors of various hotels as members migrate from one hospitality suite to another while people who haven't met since graduation exchange abrazzos and shouts of recognition and mutual acclaim while over a martini they recapitulate twenty-five years of intervening history, boast about their children and expostulate over the good old days in medical school. In some of the hospitality suites strange little political intrigues are spawned and games of tradesmanship and minor agreements. It is all part of a system where grown men play boys' games, where amateurs behave like professionals and where much that is good in gemutlichkeit, in conviviality and in mutual exchange takes place.

The political and economic activities of AMA is the business of the House of Delegates where one hundred (±) of your elected representatives gather to consider the great issues of medicine. In many ways the heart of the matter is in the ten or so reference committees where any AMA member can testify ad infinitum (and sometimes even longer). There is much heat and sometimes even a little light.

The debate at Anaheim was vigorous. A few years ago the great issue was abortion; today it is PSRO. There were heartwarming experiences such as hearing a classmate (Marvin Shapiro U of M '43) deliver a reasoned, logical and eloquent exposition. There was oratory from all sections of the country. There were quotations from scripture, from Shakespeare and from the philosophers. There was homespun vernacular to put even Sam Ervin to shame, and in fantasy, there was even a gathering of those gray coated veterans who mustered aroung George Pickett to storm up the hill to Cemetery Ridge at Gettysburg. In the end neither the forces of creeping socialism nor those of rock hard conservatism—both were referred to—carried the day. The leadership of AMA was repudiated—but only mildly so—by the House of Delegates to make it clear that there is no Bonapartism in the AMA. On the issue of PSRO, conservative forces mostly from the South expressed the new populism, rebuked the trustees but in the end achieved consensus. The action of the House will doubtless be criticized, more outside the AMA than within, nonetheless the issue was discussed in depth and decisions whether right or wrong were not without examination.

There it is—your AMA and mine—imperfect, at times even bumbling. It sometimes obfuscates; it often delays, but it ultimately comes to grips with great issues and always arrives at conclusions aimed at preserving the best in medicine and the best in patient care.

John J Regan

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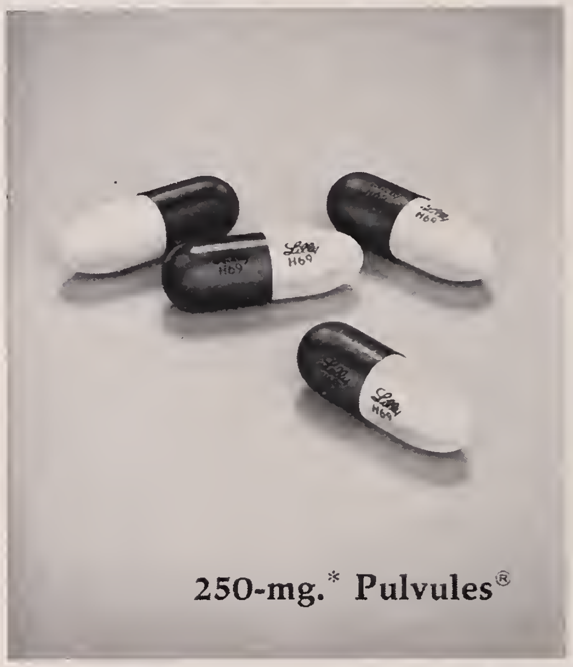

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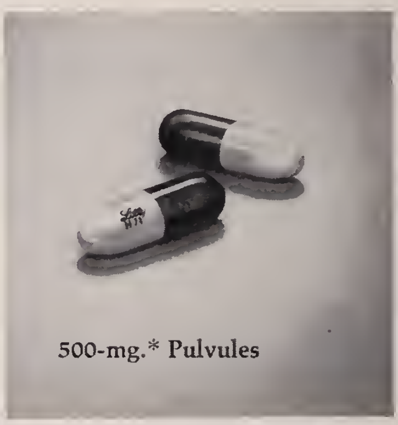

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Extractions in Hemophilia

Use of EACA

SINCLAIR G. SHORT, D.D.S.[*] and RICHARD G. OGLE, D.D.S.[*]

Through the use of EACA, the lysis of formed blood clots is prevented and good clots are formed in the presence of adequate hemoglobin and Factor VIII levels. This treatment not only decreases the cost of hospitalization, but it also decreases the risk of the patient developing antibodies to Factor VIII, hepatitis, and other sequelae associated with multiple transfusions.

THE PROBLEM OF DENTAL extractions in hemophilia is an important and formidable one. Most hemophiliacs have a well-justified dread of dental bleeding and are, therefore, reluctant to seek dental care and have characteristically suffered from dental neglect and necessity for extractions. In the past, it has been advisable to limit extractions to one or two at a time, utilizing acrylic or gutta percha splints, hospitalizations and, of course, preoperative supplementation of Factor VIII.

Blood contains not only the clotting factors that will initiate, accelerate, and limit coagulation as required, but also a series of safety devices (to prevent intravascular coagulation and lyse inappropriately formed and disadvantageously formed blood clots).

Coagulation proceeds in three phases. The first phase is the development of activated thromboplastin, which is generated within the circulating plasma, the so-called intrinsic mechanism. If the first stage occurs within the tissues, it is designated the "extrinsic portion" of Phase I. The intrinsic portion of Phase I is a slow process generating thromboplastin via a complex series of enzymatically catalyzed steps, while the extrinsic development of activated thromboplastin is a relatively rapid process. It is necessary, in vivo, that both of these phases be operational for normal hemostasis. Once activated thromboplastin has been produced, Phase II of coagulation proceeds, and prothrombin is quickly converted to thrombin. Thrombin then facilitates conversion of fibrinogen to fibrin in the third phase of coagulation.

The currently held sequence of these complex events is illustrated in Figure 1.

Hemophilia 1 or "true" hemophilia, as opposed to pseudohemophilic states, is a disease almost exclusively of males, characterized by a deficiency of Factor VIII, and is a sex-linked recessive characteristic. This disease is classically described as a manifestation of a functional de-

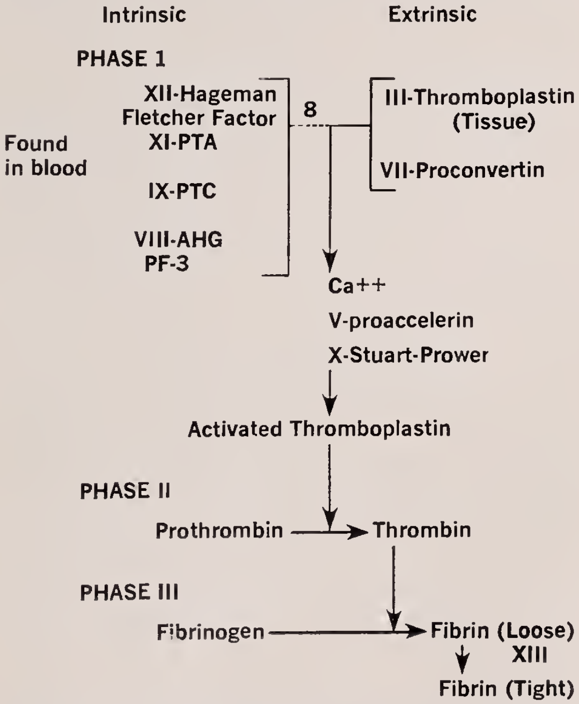

Fig. 1—Interrelationships between intrinsic blood elements and extrinsic tissue elements as they relate in the process of clotting.

---

[*] Resident, Division of Oral Surgery, University of Minnesota.

[†] Associate Professor, Division of Oral Surgery, University of Minnesota.

ficiency of antihemophilic globulin (Factor VIII). The first and most widely accepted theory is that there is a fault in the production of a plasma protein, antihemophilic globulin. The second hypothesis is that the plasma does not lack the antihemophilic factor; rather, it appears to contain a nonfunctional variant of this clotting factor.

Clinical manifestations show all variations, from a very mild to very severe bleeding tendencies. The great majority of cases may be arbitrarily classified into two main groups, the moderate to severe and the mild. In the severe form, there is virtually no antihemophilic factor activity detectable in the plasma, while in the mild form, the plasma concentration of the functional antihemophilic factor may be as high as 30% of normal. Their symptoms are proportionately milder; and bleeding may occur only after such challenges as injury, operative procedures, or dental extractions.[1]

This distinction is useful, since it governs to a considerable extent their management and treatment. The moderate to severe hemophiliacs almost invariably give a history of bleeding dating from early infancy, which includes hemarthrosis, active bleeding following circumcision, dental extraction, tonsillectomy, and accidental laceration. Almost invariably, these patients give a history of multiple transfusions and hospitalizations.

The history and physical examinations are invaluable aids in suggesting a diagnosis of hemophilia. The definitive diagnosis is predicated on the quantitative assay of Factor VIII, found by using a modification of the prothrombin consumption test and quantitating the Factor VIII level as a percentage of the average normal amount.[2]

Fibrinolytic System

As illustrated in the coagulation scheme in Figure 1 and in the foregoing discussion, hemophilia has, in the past, been defined as bleeding on the basis of deficient Factor VIII and its influence on intrinsic plasma coagulation. Recent investigation into fibrinolytic disorders has indicated this mechanism may be a possible secondary cause for abnormal bleeding in the hemophilic patient.

Activation of the plasminogen-plasmin system results in fibrinolysis. Plasminogen, a naturally occurring globulin, can be converted to plasmin, a proteolytic enzyme, by certain activators such as urokinase, streptokinase, and tissue and plasma-activating substances. Plasmin digests fibrin, forming numerous soluble fragments.[3]

Plasminogen, found in body fluids and secretions, has its highest concentration in plasma; the plasminogen activators are concentrated in the body tissues and vascular endothelium.

Plasmin is an endopeptide which intensively digests fibrinogen and fibrin in a similar chemical manner. It also rapidly attacks other biologically important proteins, including antihemophilic Factor VIII and accelerator globulin (Factor V).[3] This knowledge led to the hypothesis that therapy which would neutralize this system might also assist hemophilic patients in reducing their hemorrhagic problems.

Fibrinolysis in man is a controlled and regulated process which tends to be continuously active and dynamic in response to stimuli. The controlling factors are plasma inhibitors which, while present, tend to deactivate plasminogen activators, thus keeping the system in balance. Only when there are prolonged or sustained plasminogen activators present does the fibrinolytic mechanism then follow its course to the dissolution of fibrinogen and the fibrin clots.[3]

There are two major types of fibrinolytic disorders, a primary and a secondary form. The primary form concerns a sustained increase in plasma proteolytic activity sufficient to digest large amounts of circulating fibrinogen. The secondary form is either a response to, or an association with, intravascular clotting or defibrination.[3]

Primary fibrinolysis can be produced by three mechanisms. The first is increased amounts of plasminogen activators, urokinase or streptokinase. These substances can be given therapeutically, or released endogeneously from activator-rich neoplastic tissues such as prostatic carcinoma, or occur as a response to profound stimuli such as severe shock, injury, lung surgery, or premature separation of the placenta.[3,4] This temporarily allows sustained levels of plasmin to overwhelm the normal plasma inhibitory mechanism. Second, with disease states such as cirrhosis, deficiencies in inhibitory mechanisms may exist and activator cannot be cleared from the circulation. Finally, other proteolytic enzymes may be produced by disease states, such as some types of leukemia which produce a similar state also capable of degrading fibrinogen.[3]

All three phases, either singularly or in combination, allow the fibrinolytic mechanism to proceed to the stage of fibrinogen and fibrin dissolution.

To neutralize this system, before, during, and after dental extraction in hemophiliac patients, epsilon aminocaproic acid (EACA) is utilized and is highly successful.[5,6] EACA inhibits fibrinolysis at two sites. First, through antiplasmin activity it inhibits the enzyme plasmin from hydrolyzing the fibrin clot. Secondly, through the inhibition of plasminogen activator, EACA blocks the conversion of plasminogen to plasmin[7] as illustrated in Figure 2.

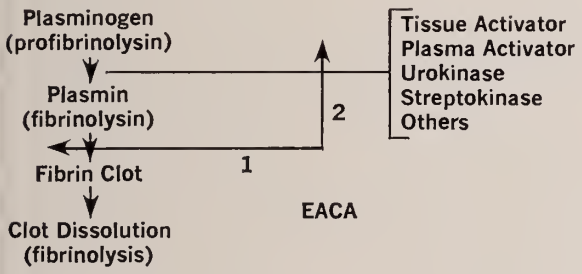

Fig. 2—Clot Lysis.[7]

Since the possibility exists that the fibrinolytic system is activated in cases of hemophilia, EACA is now utilized in conjunction with cryoprecipitated Factor VIII in the treatment of hemorrhaging hemophiliacs. The addition of EACA also allows one to reduce the number of units of cryoprecipitate necessary to maintain normal clotting function.

The following case report illustrates the clinical application of EACA in patient management.

Case Report

A 45-year-old white male was referred to the University of Minnesota Hospitals by his physician for "spontaneous hemorrhage from an infected tooth."

The Department of Hematology requested Oral Surgery to review and evaluate the patient's oral condition. Removal of the patient's remaining 24 teeth was necessary because of gross dental sepsis.

Initial care of the patient included therapy with cryoprecipitated Factor VIII and whole blood. The patient's hemoglobin increased from 7.1 to 9.7 grams/100 ml. and the Factor VIII level increased from 18% to 84%. EACA administration was started in conjunction with cryoprecipitated Factor VIII to decrease the need for this blood factor.

Surgery was completed 18 days after admission following hematologic stabilization. Prior to the surgery, 42 units of cryoprecipitated Factor VIII were given. Presurgical determination for Factor VIII was a suboptimal surgical level of 68%.

Surgery proceeded utilizing oral endotracheal intubation. During the procedure, all remaining teeth were removed with forceps and elevator technique without bone removal. Wounds were closed with interrupted 3-0 plain gut sutures with an estimated blood loss of 150 cc.

Immediately after the procedure, 20 units of cryoprecipitated Factor VIII were administered, elevating the Factor VIII level to 100%.

During the postoperative period, there was no hemorrhage from the wound sites beyond what one would expect from a normal patient undergoing a similar surgical procedure.

Five days postoperatively, the Factor VIII was determined and the level was 14%. The hematologist stated that, in similar patients, he would have anticipated a minimum Factor VIII level of 30-40% would be necessary to prevent postoperative bleeding, rather than the 14% that was exhibited by our patient.

The patient was managed only with EACA for the remainder of his six-day hospital stay.

Eleven days postsurgically, there were still no signs of hemorrhage, and the patient was discharged and instructed to continue his EACA medication for an additional six days.

Discussion

In the past, it was felt that hemophilia was only associated with a deficiency of Factor VIII, but recent considerations of the fibrinolytic disorders indicates this mechanism may be a possible adjunct to abnormal bleeding episodes encountered in the hemophilic patient.

Fibrinolysis is a controlled and regulated process which tends to be continuously active and dynamic in response to stimuli. To control this system, plasma inhibitors are present which tend to deactivate plasminogen activators and keep the system in balance.

When an imbalance in this system is produced, the fibrinolytic mechanism causes the dissolution of fibrin and abnormal bleeding episodes ensue. Activation of this system has been noted in prostatic carcinoma, severe shock or injury, lung surgery, or premature separation of placental tissue. To control bleeding episodes in these circumstances, EACA has been utilized successfully (EACA acting through antiplasmin activity and through the blockage of plasminogen conversion to plasmin). With this background we have implemented the use of EACA in management of dental extraction in hemophiliac patients.

With the concept in mind that the fibrinolytic system may be activated in hemophiliacs in conjunction with surgical injury or through some interrelationship of abnormal Factor VIII production or quality, EACA is added to the cryoprecipitated factor regimen.

It is still necessary to elevate the Factor VIII level to optimum levels prior to surgical intervention so that normal clotting will occur. With the use of EACA, investigators and clinicians are noticing more stable clots and that the Factor VIII level does not have to be as high to prevent bleeding episodes.

This would suggest that some phase of the fibrinolytic mechanism is present in hemophiliacs, and that EACA adequately controls the situation, allowing the blood clots to maintain their initial integrity. This control is so well documented that some individuals even suggest simple extraction procedures be performed with the use of EACA alone.

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The program is acceptable for ten (10) elective hours by the American Academy of Family Physicians.

	Introduction and Basics Moderator—Allan Kind, M.D.
8:00 - 9:00 a.m.	Antibiotic Choices—1974 Marvin Turck, M.D. University of Washington, Seattle
9:00 - 10:00 a.m.	Laboratory Help in Infection Problems John Matsen, M.D. University of Minnesota Medical School
10:00 - 10:20 a.m.	Coffee Break
10:20 - 11:00 a.m.	Anaerobic Infections and Post-operative Abdominal Sepsis Ronald Nichols, M.D. Veterans Administration West Side Hospital, Chicago
11:00 - 12 Noon	Case Presentations and Discussion
12:00 - 1:00 p.m.	Lunch
1:00 - 2:00 p.m.	Presentation of Interesting Infection Problems Marvin Turck, M.D. Ronald Nichols, M.D.
	Antibiotics in Elective Surgery Moderator—Ramon Gustilo, M.D.
2:00 - 2:30 p.m.	Cardiovascular Surgery Wendall Hall, M.D. Veterans Administration Hospital, Minneapolis
2:30 - 3:00 p.m.	Orthopedic Surgery Ramon Gustilo, M.D. Allan Kind, M.D.
3:20 - 4:00 p.m.	General Surgery Ronald Nichols, M.D.
4:00 - 4:30 p.m.	GU & GYN Surgery Marvin Turck, M.D.
4:30 p.m.	Case Presentations and Discussion
	Saturday, February 23, 1974 *Moderator—Allan Kind, M.D.*
8:00 - 9:00 a.m.	Medical and Surgical Chest Conference Informal Case Presentations—Marvin Turck, M.D.
9:00 - 9:30 a.m.	Osteomyelitis Patrick Kelly, M.D. Mayo Clinic, Rochester, Minnesota
9:50 - 10:30 a.m.	Gram Negative Sepsis Marvin Turck, M.D.
10:30 - 11:15 a.m.	Gas Gangrene Claude Hitchcock, M.D. Hennepin County General Hospital, Minneapolis

Isoniazid Toxicity

Reversal with Pyridoxine

PATRICK E. MOTTRAM, M.D.,* PAUL B. JOHNSON, M.D.† and
JAMES E. HOFFMAN, M.D.†

Case report of isoniazid toxicity following ingestion.

ISONIAZID (INH) TOXICITY following accidental ingestion and attempted suicide has been previously reported.[4,5,9] This case report is, to our knowledge, one of the first in which the readily available anti-tuberculous drug, INH, was willfully taken in excess without an awareness of potential toxic effects.

With the widespread therapeutic use of isoniazid and equally widespread "trials" of drugs by individuals in our society, cases similar to this may become more common and the need for recognition more pressing.

Case Report

A 17-year-old male, was admitted to St. Paul-Ramsey Hospital approximately five hours after ingesting 15 to 20 300 mg. INH tablets which he had "found" on a bathroom shelf. Within an hour following the ingestion of the tablets, the subject was described as becoming "hyperexcitable." and hyperactive. This sequentially progressed to states of confusion, violence, and finally semistupor. On presentation, he was described as semicomatose and was noted while in the emergency room to have a single grand mal convulsion. This seizure was readily controlled by the administration of diazepam, 10 mg. intravenously. No previous history of seizure disorder could be subsequently elicited. A blood pressure was initially recorded as 160/92, pulse 130 min. and irregular, and respiratory rate 30/min. The remainder of the physical examination was considered to be normal. An electrocardiogram done at the time revealed atrial fibrillation with no other abnormalities. The temperature taken rectally on two occasions was 97° F.

Blood samples taken at this time and serially after admission are shown in the Table. Initial studies recorded at 3:00 P.M. were drawn in the emergency area.

The toxicology screen drawn at 3:00 P.M. was negative for barbiturates, opiates, and amphetamines.

At 5:00 P.M. after the review of laboratory findings, the patient was arbitrarily given 100 mg. of pyridoxine intramuscularly. No seizures other than that noted initially occurred during his hospitalization. Within an hour the subject, although lethargic, could respond appropriately to questioning. By 8:00 P.M., his vital signs were stable and he was reported to be both alert and well oriented.

At time of discharge, there were no neurological or metabolic sequelae. Arrangements were made at this time for further psychiatric counseling.

Discussion

Earlier reports have shown isoniazid to be

TABLE
Acute Course of G.G.

		10/4				10/5	10/7
	2 P.M.	3 P.M.	5 P.M.	6 P.M.	8 P.M.	1:30 A.M.	
	INH ingestion		Pyridoxine 100 mg. IM				
Na		139		127	132	140	139
K		3.6		4.7	3.3	3.7	4.6
Cl		96		96	102	108	101
HCO_3		<10		<10	13.1	15.3	21.5
Anion gap		37-47		26-36	20	20	20
Glucose		444		390	146	83	100
Lactate				52.2 (nl. 9-16 meq.)			
Serum Ketones		Neg.			Neg.		
Urine Ketones		Neg.			Neg.		
pH		7.05		7.26	7.36		
pCO_2		20		31	32		
pO_2		113		93	84		

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rapidly absorbed from the gastro-intestinal tract reaching peak serum levels in approximately one to six hours.[1,2] There appears to be no significant "blood-brain" barrier as cerebrospinal fluid drug levels closely parallel levels simultaneously measured in the serum.[2] The specific levels of isoniazid that have been previously reported by other authors appear to be directly proportional to the dose ingested. There is, however, poor correlation between these measured serum levels of INH and the clinical features noted in the subjects who have taken the drug. Death has been reported to occur in an adult who ingested only 2 grams, while survival appears to be the rule in children who, on a calculated milligram per kilogram basis, have ingested larger quantities.[3,4,5] With a history of drug abuse in our subject, we considered that the effect of INH may have been potentiated by the simultaneous ingestion of depressants such as opiates or barbiturates or that the hyperactive state was the result of amphetamines. However, the negative toxicology screen did not support this as a possible explanation for the observed clinical manifestations.

We considered that the unusual features of this case represented a state of acute pyridoxine deficiency caused by the ingestion of INH. As the basic data elucidating isoniazid-pyridoxine reaction mechanisms have been accumulated from in-vitro studies. the extrapolation of these data to the clinical features of human overdoses should be considered speculative.

With these limitations in mind, we propose the following as explanations for the observed clinical course.

Lactic Acidosis

Early studies by Lichstein demonstrated the inhibition of endogenous respiration in *M. tuberculosis* by isoniazid.[6]. He further showed that the inhibition could be reversed in-vitro by the addition of pyridoxine. Patiala noted that levels of biologically functional pyridine nucleotides fell in animals treated with isoniazid.[7] Goldman isolated isoniazid analogs of pyridine nucleotides and made the observation that the analogs were unsatisfactory as suitable electron acceptors for many pyridine nucleotides requiring oxidative enzymes, but had no inhibitory effect on reduction of DPN or TPN by specific dehydrogenases.[8] Such analogs would cause the accumulation of reduced pyridine nucleotides and by this inhibit the oxidation of a substrate such as lactate. This could explain the clinical phenomenon of lactic acidosis. Lactic acidosis was found in our patient and corrected over a five hour period following the administration of pyridoxine without the use of bicarbonate or insulin. His course is more remarkable in view of the apparent bicarbonate resistance noted by others when pyridoxine administration was delayed in the therapy of isoniazid induced lactic acidosis.[9]

Hyperglycemia

Elevated glucose levels also appears to be a common feature of isoniazid toxicity. The explanation of this phenomenon also remains speculative. However, from the preceding discussion, it becomes apparent that metabolic pathways for the utilization of glucose would be blocked. Specific steps in the Krebs cycle that require pyridine nucleotides would be impaired leading to glucose accumulation. As intracellular glucose utilization becomes impaired, insulin release decreases and glucagon secretion is enhanced. Both of these factors would cause further increases in serum glucose levels. In our patient, the noted hyperglycemia responded to pyridoxine and serum glucose decreased from 444 mg.% to 146 mg.% in five hours. Glucose levels became normal in eleven hours and remained normal during the course of hospitalization. No insulin was administered at any time.

Hypothermia

Clinically our patient was hypothermic on admission. This is a feature commonly seen in hypoglycemic individuals and subjects given the inhibitor of glucose utilization, 2-deoxy-D-glucose.[10] The latter study postulated intracellular glucopenia produced by intracellular accumulation of inhibitory amounts of 2-deoxy-D-glucose-6-phosphate and a direct effect on a thermoregulatory center in the hypothalmus leading to hypothermia. This combination of hyperglycemia and hypothermia suggests impaired utilization of intracellular glucose.

Convulsions

Seizure activity is another hallmark of isoniazid toxicity and at this point should be considered multifactorial in etiology. Our inability to document a seizure history from our subject made it unlikely the quantity of isoniazid he ingested unmasked a seizure disorder; however, considering the subject's reliability, such a conclusion is hazardous. Pyridoxine deficiency does account for seizures and has been reported to cause convulsions in infants.[11] In the latter report as well as others where isoniazid toxicity caused the pyridoxine deficiency, the use of standard anticonvulsant regimens has been only marginally effective in controlling seizure activity. In these cases, the administration of pyridoxine led to the control of convulsions. One proposed mechanism would be a reduction in the CNS level of gamma aminobutyric acid (GABA).[12] Pyridoxine is required for the decarboxylation of glutamic acid to GABA. Experimentally the seizures associated with this enzymatic block can be ablated with pyridoxine. The lack of significant blood-brain barrier to isoniazid may also explain the observed rapid onset of seizures in individuals intoxicated with isoniazid. Intracellular hypoglycemia may additionally be a factor in leading to the development of seizures.

In our patient, the response to diazepam was unexpected and can best be explained as a nonspecific effect in an individual whose drug level was not exceedingly elevated or whose tolerance for undetermined reasons was higher than other reported cases.

In this case as well as other reports, significant improvement followed the administration of pyridoxine. Our patient was unique in that rapid reversal of the observed lactic acidosis and improvement in clinical status followed the administration of pyridoxine alone. We are unable to explain this course unless the early recognition and treatment of the disorder with pyridoxine was the significant factor in the rapid improvement.

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Cover Photo

"Morning's First Run"

Dr. John Wendland told the editors that even though the ski equipment shown in the cover photo has changed since it was taken 12 years ago, the scene at the top of Baldy Mountain at Sun Valley is just as beautiful. "The ski poles are now shorter; the bindings have changed and the boots are higher."

Dr. Wendland is an ophthalmologist practicing in Minneapolis and is well known by the readers of MINNESOTA MEDICINE for his field of corn on the November, 1972 issue which was selected as the outstanding cover of MINNESOTA MEDICINE for that year.

Serial Liver Scanning

Metastatic Disease

TIMOTHY E. TULLY, M.D.* and REX B. SHAFER, M.D.†

Five-year survival in a patient with proven hepatic metastases of carcinoma of the colon is presented. Serial liver scanning proved quite helpful in following the progress of the disease and in evaluating the response to treatment with systemic fluorouracil. As newer therapeutic modalities are tried, it is proposed that serial liver scintigraphy will permit the objective analysis of results and response to treatment.

THE LIVER is known to be a favorable milieu for the growth of malignant cells. This is especially true in the western hemisphere, where metastatic disease of the liver is at least twenty times as common as that of primary hepatoma. Carcinoma of the colon accounts for at least one-half of all the metastatic disease to the liver. Twenty-five to 50% of patients with carcinoma of the colon or rectum develop liver metastases, and when they do the outcome is almost invariably fatal.[3,10]

The survival of metastatic disease to the liver may be altered by surgical resection or systemic chemotherapeutic agents. Newer methods are now being evaluated such as liver resection, local or systemic perfusion of oncolytic drugs, radiation microspheres, and liver dearterialization. The further development of these modalities and as yet untried agents may alter the unfavorable prognosis of metastatic liver disease in the future.

A patient with a five-year survival from metastatic adenocarcinoma of the colon with lymph node and hepatic metastases at the time of original diagnosis has recently come to our attention. The value of serial liver scans following the progress of this disease and its response to treatment is dramatically illustrated by this case.

Case Report

A 40-year-old male with a one-year history of bloody diarrhea and 12 pound weight loss one month prior to admission was admitted to the Minneapolis Veterans Administration Hospital with a presumptive diagnosis of ulcerative colitis. Proctoscopy revealed a tumor at 15 cm above the anal verge. Biopsy contained adenocarcinoma. Exploration on May 22, 1968 revealed a 5 cm mass palpable in the pelvis. Exploration of the abdominal cavity was normal, except for a solitary nodule on the superior dome of the right lobe of the liver. A Silverman needle biopsy of this liver nodule showed adenocarcinoma. The nodule was not removed at this time. Anterior resection of the sigmoid colon was then performed. The surgical specimen demonstrated four of 14 regional lymph nodes to be positive. The patient was readmitted July 1968 for a five-day course of intravenous 5-fluorouracil (5-FU) (922 mg/d). He was then scheduled for readmission in January 1969 for a "second look" exploratory laparotomy. On readmission his liver function studies were normal. A liver scan in December 1969 was interpreted as normal. Hepatic arteriogram was also normal. On January 22, 1969 the patient had an exploratory laparotomy. Numerous small nodules were encountered in both lobes of the liver and an infusion catheter was placed in the common hepatic artery and intra-arterial 5-FU was administered for six days. During the next several months the patient received several courses of intravenous 5-FU. In May 1969 an intra-arterial infusion catheter was placed and a second intra-arterial course of 5-FU was given. During the ensuing four and a half years the patient received an additional 38 courses of systemic fluorouracil. His liver function studies remained normal for four and a half years, despite large fluctuating metastatic lesions seen on liver scintiphotograms (Figure). Liver scanning accurately demonstrated numerous small metastases which enlarged dramatically during the ensuing few months and then showed some improvement with treatment. The patient did well until the fall of 1972, when an elevated serum alkaline phosphatase and lactic dehydrogenase (LDH) were noted for the first time. The patient gradually developed upper abdominal discomfort and enlargement. In February 1973, he noted the onset of light stool and jaundice. On readmission, a tender hard liver was palpable. Repeat liver scan demonstrated enlargement of the metastases (Figure 1). On March 14, 1973 a hepatic artery catheter was again introduced with subsequent treatment with 5-FU.

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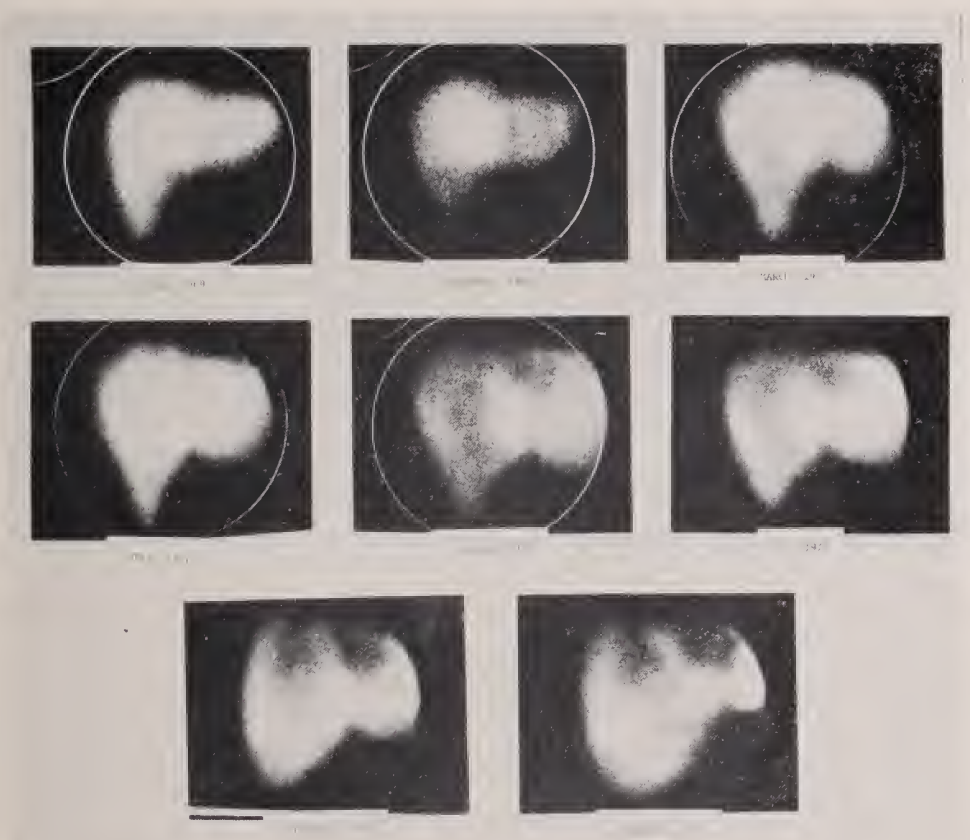
Discussion

The prognosis for patients with adenocarcinoma of the colon and hepatic metastases at the time of diagnosis is very poor.[3] Nevertheless, there have been sporadic reports of five and even 10-year survival.[2,6,9] Bacon reported a mean survival of 15.1 months in patients with hepatic metastases but without peritoneal implants after palliative resection in 25 patients. This was compared with a mean survival of six months in patients who had no treatment or only diverting colostomies.[2] There were two five-year and one 10-year survivals in this series. Pestana reported on 353 patients with liver metastases with a mean survival of six months without therapy and 15.9 months after palliative resection.[9] Floyd, in a review of 1,687 cases of carcinoma of the colon and rectum in which all patients with the diagnosis were included, demonstrated less than 2% five-year survival when other organs beyond regional lymph nodes were involved with metastases.[6]

Improved success in the treatment of hepatic metastases is largely due to the development of two therapeutic modalities—surgical resection of the metastases and infusion chemotherapy. It is difficult to evaluate results of these modalities in the absence of control groups. Jaffe offered such a series which enabled him (a) to derive information about the natural history of the disease in patients with demonstrated metastases, (b) to evaluate the relative importance of hepatic metastases in determining survival and (c) to determine the value of palliative resection.[7] In his 390 patients with proven malignancies, over 50% of metastases were from carcinoma of the



Figure—Serial liver scintiscans in 45-year old male with metastatic adenocarcinoma of the colon diagnosed in May 1968. The rapid growth of metastatic foci from June to December 1969 is evident. An apparent decrease in size of the major defect is seen in July 1971. Relapse in January 1972 followed by some improvement in May 1972 is seen. From this time to February 1973, there is progressive increase in the size of the metastatic foci—paralleling the patient's clinical course.

colon. The mean survival was 75 days after establishment of the diagnosis of liver metastases. Only 6.6% of patients survived one year and three patients survived three years. The mean survival for colonic-rectal primary tumor was 146 days, while in tumors of the biliary tract, stomach and pancreas the mean survival was 60 days. Palliative resection or diversion improved survival to 160 days, as opposed to 37 days in patients with exploration only. Survival varied inversely with the gross extent of the hepatic metastases and the magnitude of the clinical and laboratory evidence of liver impairment.

Chemotherapeutic agents have been vigorously tested in an attempt to increase survival and decrease morbidity. The survival of patients treated with systemic fluorouracil for hepatic metastases was recently reviewed by Rapoport and Burleson.[10] In 61 patients with colonic-rectal metastases to the liver treated with 5-FU, the mean survival was 11.6 months and the longest individual survival was 28 months. Response to treatment was evaluated by change in the liver size. Objective response was noted in only five patients. There was no evidence of significant increase in survival, nor did the agents offer any high probability of objective or subjective response. Indeed, its ineffectiveness when used systemically via the intravenous route, has stimulated the development of intra-arterial perfusion techniques. Ariel reported on 35 patients with metastases to the liver from colon and rectal primary tumors treated with 5-FU. There was no significant increase in life expectancy. However, 30% of patients displayed some subjective response and 10% displayed tumor shrinkage of 50% or more. Subjective response was a decrease in the symptoms of pain, anorexia and feeling of bloatiness. The lack of effectiveness of 5-FU has prompted this group to use the agent only in symptomatic patients.[1] The actual value of systemic chemotherapeutic agents in patients with hepatic metastases remains unclear. However, certain individuals have shown dramatic and prolonged improvement with the prodigious use of 5-FU.

The value of hepatic scanning in the assessment of metastatic liver disease is well accepted.[5,8] Its reliability was emphasized by Castagna, who found the overall accuracy of liver scanning in patients with carcinoma of the colon was 75% with 14% false positives and 11% false negatives.[4] In the same series of 101 patients without jaundice, the serum alkaline phosphatase was found the most reliable indicator of hepatic metastases, being abnormal in 58% of patients with metastases and normal in 88% of those without. In 18 patients with normal liver function, four had metastases as judged by liver scans. Liver scanning or hepatic function studies alone may be misleading in predicting the presence of metastases. The only absolute diagnostic certainty comes from biopsy or autopsy. The combination of scanning and laboratory data can virtually assure the correct diagnosis of metastases when both are clearly abnormal. The case in point illustrates the usefulness of serial liver scanning in accurately predicting the growth of metastatic foci in this patient and estimating the response to the treatment given. The usefulness of serial liver scanning in following patients with known metastases and its use for objective assessment of response to treatment has not been stressed in the literature. As new therapeutic modalities are developed, serial liver scanning should be used routinely to evaluate objective response to therapy and to follow the progress of the disease.

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Localization of Substernal Parathyroid Adenomas

by Venous Catheterization

ARNOLD W. LINDALL, M.D., PH.D.* AND EDWARD T. WONG, M.D.†

Parathyroid localization.

THE LOCALIZATION of parathyroid adenomas at surgery is often a difficult procedure because of the wide anatomic variation in the location of these structures. Fortunately the majority (75%) of these tumors are in the neck; 20% are in the high mediastinum, accessible from the neck, and only about 5% of these require sternotomy to be reached.

In our experience (1970-1972) with known parathyroid adenomas, we know of only three substernal adenomas in 50 cases where parathyroid hormone was measured. In one case the tumor was discovered at post mortem examination. In the other two cases a neck exploration failed to find the offending tissue and the physician consulted the authors about further steps in defining the location of the tissue. It was recommended that a remeasurement of serum immunoreactive parathyroid hormone (iPTH) be done, and if the value was still elevated, a venous catheterization be done to obtain samples from defined locations of the neck, chest and periphery.

This report deals with the venous iPTH patterns in these two cases.

Methods

Patients

Case 1

A 70-year-old woman with a history of hypercalcemia for six months prior to surgery was hypertensive and had considerable emotional lability, anorexia and insomnia. A past history of thyroidectomy for hyperthyroidism was also recorded. Her serum calciums ranged from 11.4 to 12.4 mg% before the first neck surgery, and from 11.1 to 12.1 mg% after the first surgery.

Case 2

A 24-year-old man in whom hypercalcemia in the range of 13.5 mg% was observed while he was being investigated for complaints of chest pain, nocturia and mild epigastric distress. Serum iPTH was then found to be elevated and he was submitted to a neck exploration. A cure was not affected; the patient remained hypercalcemic with abnormally high iPTH.

Venous Catheterization

The patient (Case 1) was admitted to the University of Minnesota Hospital for venous catheterization; patient (Case 2) was studied at Northwestern Hospital. Since our experience is still small, the physicians performing the catheterization were advised to obtain samples from the following sites: right superior thyroid vein or neighboring internal jugular, right internal jugular (low), right innominate vein, right subclavian vein, left superior thyroid vein or neighboring internal jugular left internal jugular vein, left innominate vein, and if possible, both right and left inferior thyroid veins, which come into this area, superior vena cava, inferior vena cava above kidneys and inferior vena cava below kidneys.

Radioimmunoassay of Parathyroid Hormone

This procedure is a double antibody technique developed at the Minneapolis Medical Research Foundation (research laboratory at Hennepin County General Hospital), and at the Metropolitan Reference Laboratory (Minneapolis War Memorial Blood Bank). It is sensitive enough to measure serum iPTH in 25 to 50 microliters of serum. The complete details of the assay procedure are available to anyone interested.

Results

The values for iPTH in both patients are shown

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Please send all communications to: Dr. Arnold W. Lindall, Director, Metropolitan Reference Laboratory, (Minneapolis War Memorial Blood Bank), 2304 Park Avenue South, Minneapolis, Minnesota 55404.

TABLE
IMMUNOREACTIVE PARATHYROID HORMONE IN VENOUS CATHETERIZATION SPECIMENS FROM TWO CASES OF SUBSTERNAL PARATHYROID ADENOMAS

	E.B. iPTH ng/ml*	C.B. iPTH ng/ml
Right internal jugular vein (high)		4.9
Right internal jugular vein (low)	5.2	4.9
Right innominate vein	8.1	6.5
Right subclavian vein	2.5	5.4
Left internal jugular vein (high)		5.2
Left internal jugular vein (low)	6.8	5.4
Left innominate vein	3.0	
Left subclavian vein	6.0	5.4
Superior vena cava	7.6	9.2
Inferior vena cava	5.4	4.9

*Normal range up to 1.5 nanograms/ml.

in the Table. In Case 1, the highest values were in the right innominate vein, and superior vena cava, closely followed by the left internal jugular (low). This pattern suggested the presence of the parathyroid adenoma in the mediastinum secreting into the right innominate vein and superior vena cava; however the relatively high value in the left internal jugular vein (low) did raise the question of the adenoma being located low in the neck. The surgeon re-explored the neck, and finding no adenoma, he then entered the chest where a four gram adenoma was found in the thymus near the root of the aorta. This gland was evidently secreting into the superior vena cava and right innominate vein, based on the iPTH profiles.

In the second case, there was a much better localization with almost a two-fold higher concentration of iPTH in the superior vena cava compared to the other values. The next highest value was in the right innominate vein. At surgery the gland was also located in the thymus within the thoracic cavity. Again, the gland appeared to be secreting into the superior vena cava and the right innominate vein.

Discussion

There will probably be an increasing demand for venous catheterization studies to aid in localization of parathyroid glands for the surgeon. Since so few glands are in the chest, it seems unlikely that such studies would routinely be done prior to the first surgery for a parathyroid adenoma. Yet the problems of localization by venous catheterization are probably compounded by rearrangements of the blood supply following an extensive neck exploration.

Venous drainage of parathyroid glands has been investigated by radiopaque dye contrast studies during inferior thyroid artery injection.[2] In most cases it was observed that principle drainage occurred into ipsilateral inferior thyroid veins. Both inferior thyroid veins enter the left innominate vein. These authors refer to two of their own cases of mediastinal adenomas, and one other case where large veins from the gland apparently entered the left innominate vein. Reitz et al.[1] reported a case of mediastinal adenoma with gradients in the right innominate and superior vena cava.

It also has been shown that to be successful in localization of neck adenomas, the catheter specimens should be obtained from inferior thyroid veins, since great dilution of iPTH occurs in the large veins.[3] This requires considerable skill on the part of the person manipulating the catheter. When these conditions were met, there was a good correspondence between the parathyroid adenoma site and large parathyroid hormone levels. In a large series Powell et al.[4] were able to localize the tumor prior to surgery in 100% of cases when thyroid vein samples were obtained. This is in contrast to only 56% success in localization where only large veins were sampled.

Occasionally there is difficulty drawing blood samples from small veins; the next best procedure is to obtain the specimen at the orifice of the vein. In all of the studies mentioned, the drainage tended to be ipsilateral.

It would seem that with all of the experience noted as well as that of O'Riordan et al.,[5] most of the guidelines are established for this procedure. In the future a venous catheterization should not be considered definitive unless left and right inferior thyroid vein samples as well as samples from large veins are obtained.

References 1-5 will be found on page 83.

Office Bacteriology

DANIEL C. MERRILL, M.D.,* COLIN MARKLAND, M.D.* and
ELWIN E. FRALEY, M.D.*

Office urine cultures are simple to perform, inexpensive, and accurate. A urine culture may be performed for 65 cents and drug sensitivity testing can be obtained, when infected, for an additional 50 cents. Although we prefer the Uro-Checkit, other techniques such as Testuria and Dipinoc seem to be equally good methods for detecting urinary tract infections in the physician's office.

CLINICIANS HAVE long recognized the need for a rapid inexpensive method to detect urinary tract nfections. Unfortunately, microscopic examination of the urinary sediment, which previously fulfilled this requirement in many office laboratories, has now been shown to be an unreliable method to detect bacteriuria.[1-3] Similarly, tests which rely on bacterial induced chemical changes in the urine have proven to be impractical due to the high rate of false positives and false negatives.[4-6] Recently several commercial firms have marketed inexpensive kits which may be used to culture organisms from the ear, throat, vagina, and urine. These culture techniques are designed for office practice and are especially useful in the diagnosis and treatment of uncomplicated (absence of obstruction, calculi, vesicoureteral reflux, etc.) urinary tract infections. Theoretically, the various techniques for office bacteriology should give a high degree of accuracy since the potentially infected material is cultured on sterile agar blocks similar to the culture media employed by most hospital laboratories. The Bacti-Lab[†] kits we tested were designed to determine the type of organism, the number of organisms, and the relative sensitivity of the organism to 12 different antibiotics.

Materials

The Bacti-Lab Uro-Checkit contains a sterile plastic container for collecting the urine sample, a label, a sterile dropper, and a culture plate with compartments for determining colony counts on ten separate urine specimens (Figure 1). The Uro-Checkit, which provides cultures at 65 cents a test, may be stored at room temperature.

The Bacti-Lab Uro-Plate has individual sections containing blood agar, Eosin Methylene blue

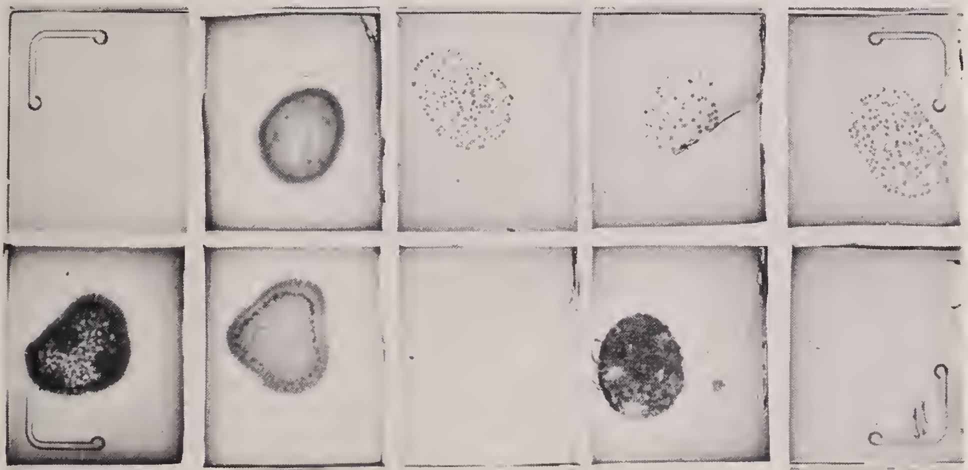

Fig. 1—The Uro-Checkit showing in the upper row from left to right urine cultures which were (1) sterile, (2) positive (>100,000 col/ml) (3) questionable (10-100,000 col/ml), (4) questionable, and (5) questionable. The lower five cultures from left to right were (1) positive, (2) positive, (3) sterile, (4) positive, and (5) sterile.

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†Bacti-Lab, P.O. Box 1179, Mountain View, California 94040.

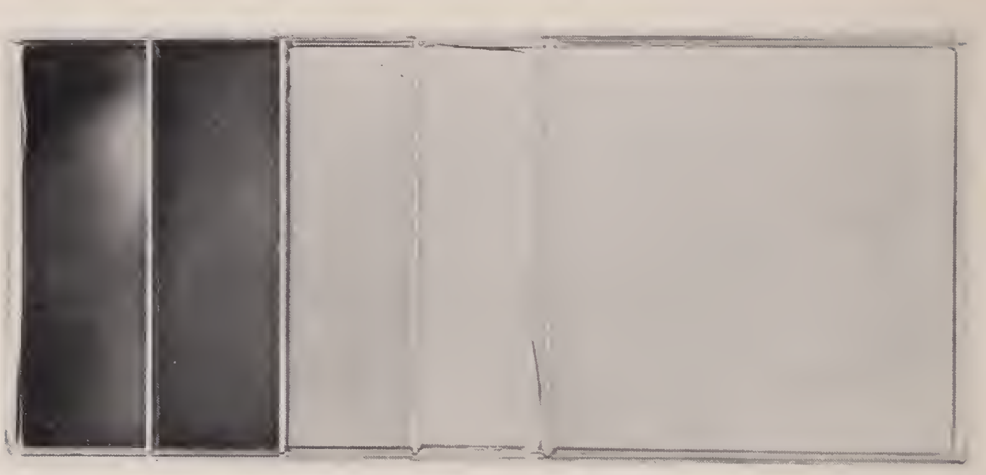

Fig. 2—A Bacti-Lab Uro-Plate.

agar, triple sugar iron agar, and urea agar which are necessary for organism identification plus an expanded section containing Mueller-Hinton Agar for drug sensitivity testing (Figure 2). The Uro-Plate costs $3.50 and it must be stored in the refrigerator and incubated during culture. An automatic drug disc dispenser* (Figure 3) was used to dispense 12 different sensi-discs† on the Mueller-Hinton portion of the Uro-Plate.

Method

Midstream clean catch urine specimens were obtained from 300 consecutive urology outpatients at the University of Minnesota Hospitals. One-half of the specimen was transferred to the sterile container provided in the Uro-Checkit and the remaining portion was sent to the hospital laboratory for culture and drug sensitivity testing. One drop of urine from the office sample was cultured on the Uro-Checkit and the remaining portion was refrigerated immediately. The Uro-Checkit culture was examined in eight to 24 hours and if positive, a portion of the refrigerated urine specimen was then recultured on the Uro-Plate for organism identification and drug sensitivity testing. Thus, in patients infected with large numbers of rapidly proliferating organisms the results from both tests often were available within 24 hours.

We employed the method McLin[7] described for determining drug sensitivity; wherein, the presence of a clear zone around the drug disc indicates antibiotic sensitivity and the absence of a clear zone indicates drug resistance (Figure 3). McLin's modification greatly simplifies drug sensitivity testing since the zone of inhibition is not measured and compared to previously determined controls. This change in methodology seems to be justified since the concentration of antibiotics achieved in the urine is usually much higher than that produced in the culture media by the sensi-discs. The presence or absence of a clear zone cannot be used to determine bacterial sensitivity to the sulfonamides which only produces complete inhibition after several generations of bacterium; therefore, when sulfonamide sensi-discs are tested, an area of decreased growth rather than a distinct clear zone is used to indicate sensitivity to the drug.

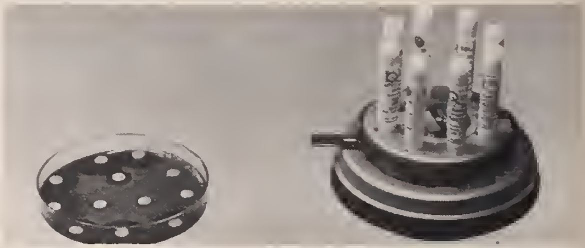

Fig. 3—A Mueller-Hinton agar plate showing clear zones which indicate drug sensitivity around several of the drug discs. The two drug discs on the right which do not have clear zones suggest antibiotic resistance. An automatic drug disc dispenser is also shown.

All office bacteriological studies were performed by a technician with only a high school education and no prior training in bacteriology.

Results

A positive culture was defined as a urine sample which produced >100,000 colonies of bacteria per ml. Colony counts between 10.000 and 100,000 were considered to represent questionable infections while urine samples which produced less than 10,000 colonies were thought to be contaminated.

Mixed Cultures

The hospital laboratory reported four mixed cultures. Examination of the Uro-Plate suggested multiple organisms in three of the four cultures. A catheterized specimen, before treatment with antibiotics, from each of the latter three patients was sterile.

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*Dispense-O-Disc, Difco Laboratories, Detroit, Michigan.

†Baltimore Biological Laboratory, Cockeysville, Maryland 21030.

Colony Counts

Sterile urine samples were reported by both the hospital laboratory and Uro-Checkit in 249 (83%) of the 300 patients. The hospital laboratory reported a positive culture (>100,000 colonies/ml) in 44 patients. The Uro-Checkit was positive in 41 of the latter group of patients and sterile or contaminated (<10,000 col/ml) in three patients. In no patient was the Uro-Checkit culture positive and the hospital culture negative. Seven additional patients were reported to have cultures with colony counts between 10,000 and 100,000 by both the office and hospital laboratory. Thus, the overall correlation between Uro-Checkit and hospital colony counts was 99 percent.

Organism Identification

The three cultures reported to be positive by the hospital laboratory and negative by the Uro-Checkit culture were eliminated from this portion of the study. Identical organisms were reported by both culture techniques in 27 (66%) of the 41 cultures The organisms falsely identified by Uro-Plate included Serratia in two cultures, Staphylococcus aureus and Streptococcus faecalis in two cultures each, and Candida in one culture. A different gram negative organism was isolated by the two methods on seven occasions.

Drug Sensitivity Testing

Since the office method tested all bacterium to the same 12 drug discs while the hospital laboratory determined drug sensitivity only for those antibiotics to which the organism was likely to be sensitive, there were many instances in which the two methods tested different antibiotics. When both facilities did test the same antibiotic, identical results were reported in 95 percent of the tests.

Discussion

Interest in office bacteriology is a natural outgrowth of the inherent disadvantages of standard hospital laboratories methodology which include: (1) the inconvenience of transporting either the patient or the specimen to the laboratory; (2) the inconvenience of waiting 48 or more hours for a complete report including antibiotic sensitivity; (3) the inconvenience associated with trying to obtain the report; and (4) the cost which varies between $15 and $25 in most institutions. Office bacteriology to be a significant improvement, must eliminate these disadvantages and be reasonably accurate.

The Bacti-Lab method we studied fulfills these requirements. Even though our technician had no previous training in laboratory medicine or bacteriology there was excellent correlation (99%) between the colony counts produced by the Uro-Checkit method and the hospital laboratory. In fact, one might question the significance of the three by false negative office cultures since there is more chance of contamination during transportation of the urine specimen to the hospital laboratory than there is if the specimen is cultured immediately in the office. There was also satisfactory correlation between office and hospital laboratory drug sensitivity testing. The latter result could be predicted since both facilities employ similar drug sensi-discs. McLin's method which relys on the presence or absence of a clear zone around the Sensi-disc rather than the diameter of the inhibition zone did not decrease our ability to determine antibiotic sensitivity appreciably.

Using the Bacti-Lab Uro-Plates our technician, however, was unable to identify or identify incorrectly the offending organism in 34 percent of the positive cultures. Furthermore, her ability to identify the correct bacteria present did not improve substantially with experience. We conclude, contrary to the experience of Narins,[8] that organism identification is not easy or practical for untrained personnel.

Fortunately, as pointed out by McLin,[7] identification of the offending bacteria usually is not necessary to effectively diagnose and treat the uncomplicated urinary tract infections encountered in office practice. At present we culture all urine samples on the Uro-Checkit Plate as described above. Urine specimens from patients presenting with symptoms suggestive of urinary tract infection and urine from patients with pyuria or microscopic bacteriuria are also cultured immediately on inexpensive Mueller-Hinton agar plates for drug sensitivity testing. Thus, the colony count and spectrum of drug sensitivity, the two factors necessary for treatment, are available within 24 hours in most patients who have urinary tract infection. The rare positive culture (Uro-Checkit) from an asymptomatic patient without pyuria or microscopic bacteriuria is recultured on

Mueller-Hinton plates the following day.

Our experience with other methods of office bacteriology,* in a smaller group of patients, suggests that they also are excellent methods for detecting urinary tract infections. We prefer the Uro-Checkit since the plates do not have to be refrigerated when stored or incubated when the culture is performed. Anyone interested in performing office urine cultures should also consider the office bacteriology techniques described by Stamey[1] and McLin[7] who recommend culturing the urine on a split plate containing both blood agar and desoxycholate agar. The latter culture medium inhibits the growth of gram positive organisms which may contaminate the urine. Stamey[1] also believes that organism identification usually can be accomplished by observing the growth characteristics on these two agars. We have not used the split plate technique because: (1) colony counts are more difficult (all colonies on the split plate must be counted); (2) because contaminating organisms whether gram positive or gram negative usually give a colony count of less than 10,000 and thus can be eliminated from consideration by simply estimating the number of colonies present (making the distinction between gram positive and gram negative organisms unnecessary); and (3) because organism identification is, in our hands, inaccurate.

Office bacteriology has been criticized because there are no periodic controls (unknowns) to assure continuing accuracy and because it is difficult or impossible to perform colony counts or drug sensitivity tests if more than one organism is present. The first criticism may be justified; however, test standardization probably is of less importance in an office setting where a single technician consistently performs the same procedure than it is in a large laboratory with changing personnel. The second criticism seems to have less merit since mixed cultures, which usually represent contamination in office patients, are infrequent if not rare in clean catch midstream urine samples obtained in an office where the collection technique is controlled and the urine is cultured immediately.

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*Dipinoc—Stayne, 480 Paterson Avenue, East Rutherford, New Jersey and Testuria—Ayerst Laboratories.

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Meetings

Child Psychiatry in Practice

A series of training seminars sponsored by the MSMA Committee on Psychiatric Training for Non Psychiatric Physicians.

Feb. 21—School Refusal and Learning Disorders.

Mar. 21—A Child Goes to the Hospital.

Apr. 18—The Dying Child and His Family.

May 16—Early Neurotic and Psychotic Disorders.

Mail registration to: Dorothy Bernstein, M.D., Fairview Hospital, 2312 So. Sixth St., Mpls. 55406.

The Minnesota Academy of Ophthalmology and Otolaryngology

Feb. 8—The Minnesota Club, St. Paul. The Benedict Lecture, to be announced.

Mar. 8—The Decathlon Club, Minneapolis. *Ophthalmology:* "Echography and Tissue Differentiation in Vivo." Speaker: Karl C. Ossoinig, M.D., University of Iowa, Iowa City, Iowa. *Otolaryngology:* "Dynamics of Rhinoplasty" Speaker: M. Eugene Tardy, M.D., University of Illinois.

Primary Thrombosis of the Subclavian Vein

RONALD OLIN, M.D.*

Primary or so-called effort or strain occlusion of the axillary or subclavian vein tends to occur in healthy males with well developed neck and shoulder muscles between the ages of 20 and 25 years who are commonly engaged in heavy labor. The dominant arm is usually involved and the condition develops immediately or several hours after physical effort which may seem trivial or vigorous; often there is no apparent predisposing cause. Clinical features are fully developed in 24 to 48 hours and include edema, pain, cyanosis, and increased superficial venous collaterals; constitutional disturbances are absent. The diagnosis can be confirmed by intravenous venography. Symptoms subside in a few days to a few weeks and the patient can resume light work in two or three months. Recovery can occasionally be protracted with frequent exacerbations and disability. Conservative treatment should include anticoagulants. No fatalities have been reported nor pulmonary emboli. The etiology is disputed but the popular theory advocates that when the arm is abducted at the shoulder, external compression of the vein by the costo-coracoid ligament or the subclavius muscle results in venous stasis, venospasm, and possibly thrombus formation; if the subclavio-axillary valve is ruptured, thrombus commonly forms on the damaged intima.

PRIMARY THROMBOSIS of the subclavian or axillary vein is an uncommon condition usually occurring in young, healthy individuals after sudden or unusual muscular effort. It must be distinguished from thrombophlebitis secondary to direct trauma, blood dyscrasias such as polycythemia vera, congestive heart failure, postoperative scarring, infectious phlebitis, and compression of the vein by an aneurysm or tumor. The disease was first described by Sir James Paget in 1866 and again by Von Schroetter in 1884 and bears the eponym "Paget-Schroetter syndrome." About 400 cases have been described in the literature, mostly from European writers. A comprehensive review of 320 cases was presented by Hughes in 1949.[1]

Case Report

A 19-year-old white woman, a student, was seen because of two days of swelling and discoloration of the right upper extremity.

She had started school one month previously after three months of summer vacation and did not recall any unusual physical activity other than typing for about five hours a day since returning to school. Mild discomfort in the region of the right elbow had occurred on several occasions during the previous week. Two days before being seen, moderate pain developed in the right elbow, followed by rapid swelling and discoloration of the entire right upper extremity. She had not taken any medications in the recent past other than an occasional aspirin.

The past history was not remarkable except for mild headaches of the migraine type since age 15 for which she took only aspirin. Her father once had thrombophlebitis of the lower extremity, her mother had varicose veins, and there was a positive family history of diabetes mellitus in grandparents on both sides of the family.

Examination revealed a healthy-appearing young woman in no acute distress. Vital signs were normal. There was moderate cyanosis of the right upper extremity which was one inch larger in circumference at the forearm and arm compared to the left side. The collateral superficial veins in the region of the right shoulder girdle were prominent. Arterial pulses, sensation to touch and pin-prick, deep tendon reflexes and muscle strength were normal. The axilla was not tender to palpation. Thoracic outlet maneuvers were negative. The remainder of the physical examination was not remarkable.

The hemoglobin was 15.6 gm% and leukocytes 9,450 mm^3 with a normal differential. Fasting blood sugar and routine urinalysis were normal. Chest Xray was

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The right arm being the dominant one in most persons is the one usually involved. When the left arm is affected, the patient is usually left-handed or has used the left arm in some unusual way. Edema and cyanosis of the arm are almost constant features. The superficial veins on the anterior aspect of the shoulder and chest are almost always prominent. There can be tenderness along the course of the subclavian, axillary or basilic veins and in some cases the thrombosed vein can be palpated in the axilla or above the clavicle.

Course: The acute symptoms subside in a short time, varying from a few days to a few weeks. Complete recovery both subjectively and objectively has been claimed by many observers. However, some swelling, discoloration, or obvious collateral veins are usually permanent to some degree. The usual case is able to resume light work in two to three months. In some cases, the clinical features may persist or recur often to a disabling degree. Relapses are often provoked by returning to the same type of work. Matas[2] described a case in which pain and swelling recurred each time the patient returned to work over a four year period. Veal and McFetridge[3] reported persistent recurrences in three patients followed for six, 10 and 22 years, respectively. Relapses are thought to be caused by inability of the venous collaterals to respond to increased flow rather than re-injury to the occluded vein. Several prolonged Workmen's Compensation arguments have followed with the judgment usually in favor of the patient.

Prognosis: No fatalities have occurred. It is doubtful whether pulmonary emboli have ever occurred from the disease.

Laboratory Investigation

Hemoglobin, leukocyte count, platelet count, sedimentation rate, bleeding and clotting times have been normal in almost all reported cases. Measurement of the venous pressure, circulation time, and oxygen saturation of the venous and arterial blood of the involved extremity have been used to help confirm the diagnosis and follow the course of the disease. More recent laboratory aids have included intravenous and infrared venography.

Treatment

Conservative treatment during the acute phase consists of bed rest, warm packs, elevation of the arm, simple analgesics, and anticoagulants. Elevation and warm packs help to reduce venous and arterial spasm and so decrease the edema. Anticoagulants are thought to reduce the propagation of the thrombus into tributary veins and thus aid in the development of the collateral circulation. For persistent or recurrent symptoms, a paravertebral sympathetic block has been advocated by some to assist in the development of venous collaterals.

Attempts have been made to formulate indications for surgical intervention such as rapid increase in edema, persistence of edema, and exacerbations with return to work. Surgical exploration has usually benefited the patient and has consisted of simple thrombectomy or excision of the vasospastic, thickened or thrombotic venous segment.

Pathogenesis

The etiology is disputed and many theories have been advocated. To Lowenstein in 1924[4] belongs the credit for the first exacting anatomical study and the most popular conception as to etiology. The subclavius muscle arises from the first costal cartilage and is inserted into the groove on the inferior aspect of the clavicle. The costocoracoid ligament (membrane) is a thickened sheet of deep fascia filling the gap between the subclavius muscle and pectoralis minor blending laterally into the coraco-clavicular ligaments and medially with the first and second costal cartilages. Lowenstein pointed out that the inferior border of the costo-coracoid ligament was sharp, strong and crescentic and was further strengthened by the tendinous fibers of the subclavius muscle. Both structures follow the course of the clavicle laterally and posteriorly and cross the vein. He noted that when the arm was abducted to the level of the shoulder, the costocoracoid ligament was put on the stretch exerting considerable pressure on the superior surface of the vein. This stretching or compression of the vein results in proximal venous stasis and thrombus formation or a marked venospasm. In several cases, thrombus has not been found at surgery.

Gould and Patey in 1928[5] injected plaster of Paris into the axillary and subclavian veins of post-mortem subjects, the arms of which were held in a fixed abduction position. They studied the grooves in the vein and concluded that the subclavius muscle, not the costocoracoid ligament, negative; there were no cervical ribs. An injection of 35 ml of 50% Hypaque into the right antecubital vein revealed distension of the basilic and axillary veins. There was complete obstruction of the subclavian vein with collateral filling around the obstruction (Figure).

The patient was hospitalized for one week. The right arm was immobilized, elevated and treated with continuous warm, moist packs. Heparin and Panwarfin were used.

One month after dismissal from hospital, pain was no longer present but the arm was still slightly cyanotic and enlarged. Panwarfin was discontinued after three months. Six months later the arm had returned to normal size and color. The collateral veins were still prominent. The arm otherwise felt normal except for occasional mild, sharp pains in the right shoulder region.

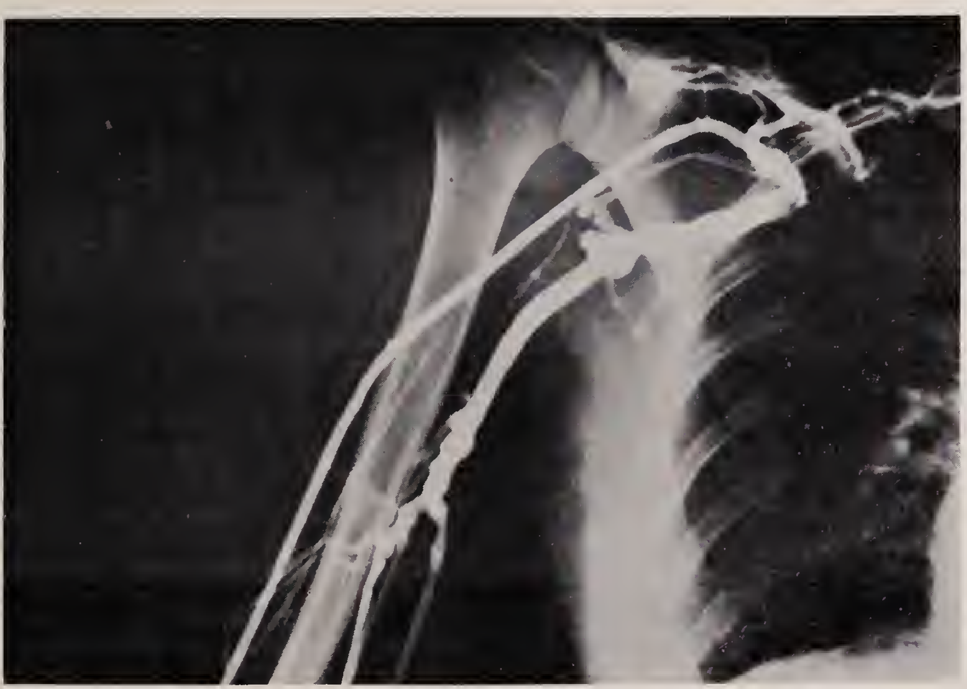
Discussion

Clinical Features

Age and Sex: The age incidence rises sharply to a maximum between 20 to 25 years and then tapers slowly. Only a few patients over age 50 develop the condition. The youngest patient reported was a girl age 11 and the oldest a man age 75. Males are more frequently affected (78% in Hughes' series). Characteristically, they have well developed shoulder and neck muscles.

Onset: The condition usually develops immediately, a few hours, or occasionally a few days after some vigorous or trivial physical effort in which the arm is fully abducted and possibly externally rotated at the shoulder. It commonly occurs in persons engaged in heavy labor in which there is a sudden strain, habitual occupational strains with a sudden extra effort or after seemingly banal accidents. No sport, occupation or activity is immune from the disease. It has been reported in tennis and squash players, golfers, base ball players, rowers, boxers, swimmers, basketball players and gymnasts. Other activities mentioned are lifting heavy weights, overstretching the arm when painting a ceiling, placing jars on a high shelf, washing clothes or dishes, vigorous stirring of a heavy Christmas pudding, beating time with a baton, swinging a sledge hammer, pushing a bed past an obstacle, ringing heavy bells in a church belfry, and simply putting an arm into an overcoat sleeve. There may be nothing to account for the onset as Hughes noted in 39 (13%) of 320 cases in which the patient awoke in the morning to find the arm swollen, blue, or painful.

Symptoms and Signs: The condition usually requires 24 to 48 hours to develop fully. The first clinical feature is usually a nonpitting edema of the arm from the hand to the shoulder girdle. Sometimes pain or cyanosis occurs at the onset. Parasthesias and pruritus may also be experienced. Systemic symptoms are almost always absent.



Figure—Hypaque injection into the right antecubital vein showing distension of the axillary and basilic veins. There is complete obstruction of the subclavian vein with considerable collateral circulation around the obstruction.

was responsible for the trauma to the vein. They also suggested that rupture of the delicate, bicuspid, subclavio-axillary valve, resulting in a roughened intima, was the fundamental pathologic lesion responsible for the development of thrombus.

Additional factors in the etiology probably include anatomic configuration regarding the shape of the clavicle and ribs, circulatory slowing and respiratory movements.

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One would have supposed that, by this time, the theme of universal admiration was lifted to the very pinnacle of popularity. No such thing. The curate began to cough; four fits of coughing one morning between Litany and the Epistle, and five in the afternoon service. Here was a discovery—the curate was consumptive. How interestingly melancholy! If the young ladies were energetic before, their sympathy and solicitude now knew no bounds. Such a man as the curate—such a dear—such a perfect love—to be consumptive! It was too much. Anonymous presents of black-currant jam, and lozenges, elastic waistcoats, bosom friends, and warm stockings, poured in upon the curate until he was as completely fitted out, with winter clothing, as if he were on the verge of an expedition to the North Pole: verbal bulletins of the state of his health were circulated throughout the parish half-a-dozen times a day; and the curate was in the very zenith of his popularity.*

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*Charles Dickens: Sketches by Boz, "The Curate." 1836.

Mesonephric Carcinoma of Cervix

A Case Associated with Intra-Uterine Pregnancy

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RAYMOND A. LEE, M.D.*; DAVID G. DECKER, M.D.* and
MALCOLM B. DOCKERTY, M.D.*

A case report of a woman with mesonephric adenocarcinoma of the cervix and pregnant at the time the tumor was discovered.

In 1966, Fawcett, Dockerty, and Hunt[1] reviewed all cases of mesonephric carcinoma of the cervix in the world literature and added 15 from the Mayo Clinic. Hameed[2] added five cases, one of which was associated with an intra-uterine pregnancy. Recently, we treated a young woman who had mesonephric adenocarcinoma of the cervix and who was pregnant when the tumor was discovered. This case represents the second case of such tumor associated with pregnancy.

Report of a Case

A 19-year-old woman was examined at the Mayo Clinic on March 20, 1972. She had been married six months and stated that her last menstrual period had been January 15, 1972. Two months prior to her examination, she had noted burning and soreness after sexual intercourse but had no vaginal bleeding. Her local physician found evidence of vaginitis and began treatment. Because of the unusual appearance of the mucosa of the vagina and cervix, biopsy specimens were taken. Pathologic diagnosis was uncertain, and tissue was submitted to the National Institutes of Health and Armed Forces Institute of Pathology. Two pathologists from these institutions interpreted the specimens as malignant, and the patient was referred to the Mayo Clinic for treatment. The patient's history revealed that, during pregnancy, her mother had received "hormones" for vaginal bleeding and had been hospitalized during that pregnancy. The patient had had a heart murmur since birth. Her only previous surgery was a tonsillectomy as a child, after which she received a blood transfusion. No other significant past history was obtained.

The examination revealed a thin young woman in good general health. A grade 2/6 systolic heart murmur was interpreted by a cardiologist as being inconsequential. All other positive physical findings were confined to the pelvis. Examination of the introitus revealed a small condyloma. A tumorous lesion involved the upper 3 cm of the vagina and the entire cervix. The uterus was approximately the size of a six-week pregnancy. The ovaries were normal in size.

Results of laboratory studies were normal; hemoglobin level 13.3 g/dl, hematocrit 39.1%, leukocyte count 6,400/cu mm, and platelet count 253,000/cu mm. Results of the serologic test were negative, and the pregnancy test was positive.

On March 28, 1972, a Wertheim hysterectomy and 80% vaginectomy was performed. The patient tolerated the procedure well, and her 10-day hospital stay was unremarkable. Six-month follow-up examination revealed that she is clinically free of malignant disease.

Pathologic Features

The pathologic specimen consisted of the uterus with a 6-cm cuff of upper vagina, right and left

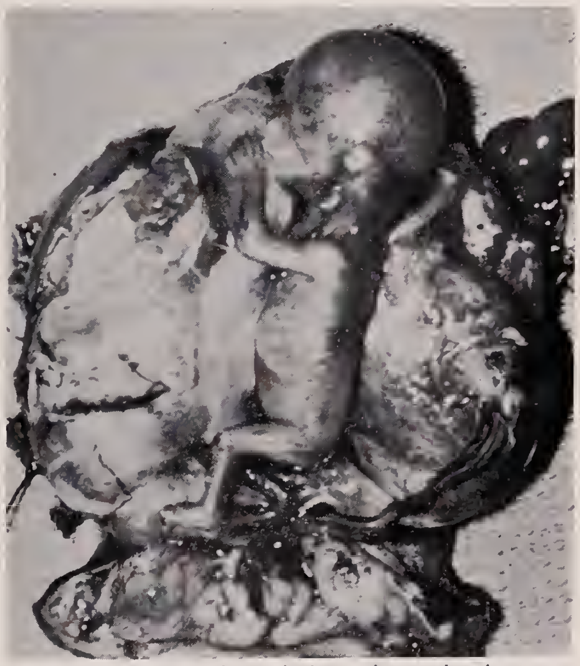

Fig. 1—Portion of surgical specimen showing pregnant uterus with polypoid cervical lesion extending to upper vagina.

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*Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

tubes, left ovary, the vermiform appendix, and pelvic nodes. In addition, there was a small verrucous lesion of the vaginal introitus.

A mixed polypoid and ulcerative malignant-appearing lesion straddled the cervicovaginal junction from approximately the 12 o'clock to the 5 o'clock position. The lesion was infiltrative in both locations, with a penetration of 1 cm into the cervix but less than this into the vaginal cuff. The pregnant uterus contained a male fetus 8 cm in length, along with its placenta and membranes (Figure 1).

Microscopically, the vaginal and cervical portions of the lesion were similar, and it was impossible to ascertain whether the growth had its origin in one structure or the other—or whether the origin was multicentric. The basic pattern was that of a grade 2 adenocarcinomatous process with foci of the intraglandular budding. The lining cells were "stubbier" than those usually seen in ordinary endocervical adenocarcinoma, and their nuclei, which varied in size and depth of staining, often projected hobnail fashion into the spaces which they lined (Figure 2 *A*). The findings fitted those described in certain cases of mesonephric carcinoma. Sections of the uninvolved vaginal cuff contained focal evidence of adenosis, with transformation of the normal nonkeratinizing squamous elements into glandular elements similar to the cells lining the endocervix (Figure 2 *B*).

The lesion of the introitus was a typical condyloma acuminatum. Pelvic nodes were normal, and the remainder of the excised tissue showed nothing worthy of special comment.

Discussion

Tumors of the cervix are rare in teen-age females.[3] Most of the lesions reported have been squamous cell epitheliomas in sexually active females. Adenocarcinomas do occur, however, and are often of the mesonephric type. Herbst and associates[4] focused attention on the clear-cell type of mesonephric tumor of the vagina and its possible induction by diethylstilbestrol. Recently, Noller, Decker, Lanier, and Kurland[5] have suggested a similar association for mesonephric carcinoma of the cervix.

Considerable effort was expended in an attempt to determine whether the patient's mother had been treated with diethylstilbestrol during her pregnancy, but to no avail. The patient's mother did have vaginal bleeding during the pregnancy and was hospitalized and given "hormones." The name and dosages are not known.

Because of the association of vaginal adenosis and mesonephric tumors, the patient has been counselled that any future change in the vaginal mucosa may be sufficient cause for total vaginectomy with a McIndoe type of reconstruction to be performed.

The prognosis for this patient should be good because we have good clearance in paravaginal and pericervical areas and the lymph nodes were negative for metastatic tumor. Recent articles[2,6] have suggested, however, that the prognosis may be better when the mesonephroma is of the purely clear-cell type than if it is of the pure Schiller or the mixed type.

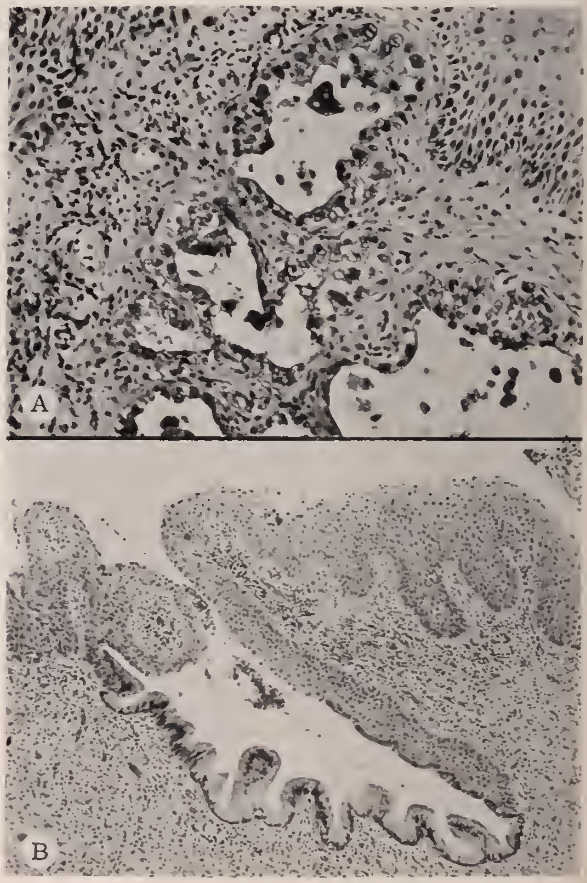

Fig. 2—*(A)* Grade 2 mesonephric carcinoma seen here ulcerating the vaginal mucosa. Growth shows coarse papillary features, and many of the malignant cells possess hobnail nuclei projecting into the spaces which they line. Cervical portion of lesion was somewhat more deeply located. (Hematoxylin and eosin; x200.) *(B)* Zone of vaginal prosoplasia showing apparent transition from squamous epithelial lining to glandular epithelium, resembling that of normal endocervix. (Hematoxylin and eosin; x100.)

In our experience with ovarian and cervical tumors of this type, the cellular "species" counted less in the prospects for long survival than did the grading of the lesion. In other words, the presence of variation of cell size and of nuclear staining, along with the degree of mitotic activity, was the important microscopic criteria in terms of patient prognosis.

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Behcet's Syndrome

Relapsing iritis and recurrent ulceration of the mouth and genitalia characterize this syndrome. Behcet in 1937 first recommended that this triad be considered an entity. It occurs chiefly in young adult males. Most of the published cases have been observed in the Near East; only three cases had been reported in the United States to 1956 (Zeavin et al.).

In addition to Behcet's triad, less common features may include: (1) cutaneous eruptions, such as acne, erythema nodosum, erythema multiforme, or furunculosis; (2) arthralgia with or without hydrarthrosis; (3) ocular disorders, such as keratitis, conjunctivitis, and hemorrhages into the retina or vitreous; (4) recurrent swelling of the salivary glands; (5) cutaneous thrombophlebitis; and (6) central nervous system disturbances, such as meningitis, encephalomyelomeningitis, paraplegia of one or more extremities, or an organic confusional syndrome.

Pathologic studies in five cases with central nervous system involvement revealed the lesions to be multiple with a predilection for the hypothalamus and brain stem. They consisted of innumerable small areas of softening observed more often in the white than in the grey matter. The etiology is not known, although a virus is suspected. Sezar in 1953 first reported the isolation of a filtrable virus from the subretinal fluid. The finding of a virus has also been reported by Evans and associates (1957). Sezar stated that a viremia is always present and that the condition is communicable. Thus far, his complement fixation tests have not been duplicated. Immunity to the disease is apparently short-llived.

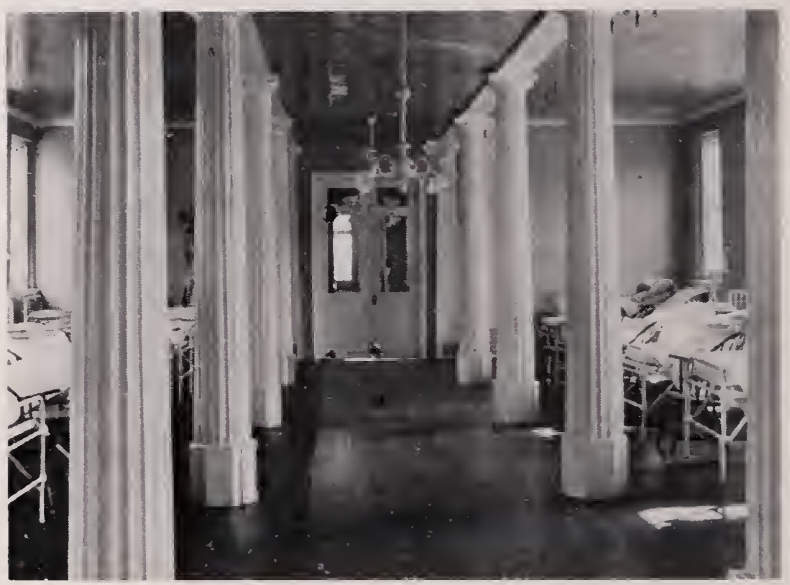
The condition runs a chronic course, in some cases as long as 20 years. Complete remission is rare. Ocular lesions are recurrent and relapsing. Both eyes may eventually be involved; and there is gradual loss of vision, sometimes progressing to total blindness. Life is endangered as a rule only when the nervous system is involved; half of such cases have proved fatal (Evans et al.). No successful treatment is known. Steroid therapy has produced temporary improvement in some cases. In lieu of a more specific type of therapy, smallpox vaccine has been recommended.

Durham, Robert H.—Encyclopedia of Medical Syndromes
Hoeber Medical Division, Harper and Row, New York

FEATURE SPECIAL

Historic Hospitals

The Pennsylvania Hospital



This photograph of Ward I in the original building of the Pennsylvania Hospital was found in a copy of Dr. Francis R. Packard's book about the hospital. A notation in his handwriting indicates that the ward has been in continuous use except for the years when Philadelphia was occupied by the British. Courtesy National Library of Medicine, Bethesda, Maryland.

The Pennsylvania Hospital at Philadelphia is older than the United States and lays claim as the first permanent hospital in the country. It was conceived in 1751 by Dr. Thomas Bond, who enlisted the famous name and promotional skill of his good friend Benjamin Franklin to bring it into being. Through Franklin's influence the Provincial Assembly incorporated the hospital early in 1751, appropriating a part of the necessary funds, the rest to be raised by public subscription. Both Franklin and Dr. Bond were members of the original Board of Managers. The proprietors of the colony, Thomas and Richard Penn, were invited to contribute land for the building and grounds. Three Philadelphia physicians, again including Dr. Bond, offered to attend the hospital free of charge for three years and to donate all the medicines needed during that time.

Although the Provincial Assembly established the hospital "for the Relief of the Sick Poor of this Province, and for the Reception and Cure of Lunaticks," it also provided for the admission of private patients "if there shall be Room in the Hospital to spare." The Assembly ruled that no incurable patients nor persons having the smallpox, itch, or other infectious distempers were to be admitted.

Lacking an endowment and receiving little revenue from patients, the hospital experienced considerable difficulty in its early financing. One source of revenue, a theatrical benefit presented in 1759, was an embarrassment to the Board of Managers, most of whose members were Quakers and therefore opposed to the theatre. The day was saved by an Episcopalian member of the board who accepted the money in the hospital's behalf.

Warren Kump, M.D.
North Memorial Hospital

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Packard, Francis R., M.D.: Some Accounts of the Pennsylvania Hospital From Its First Rise to the Beginning of the Year 1938, Engle Press, 1938.

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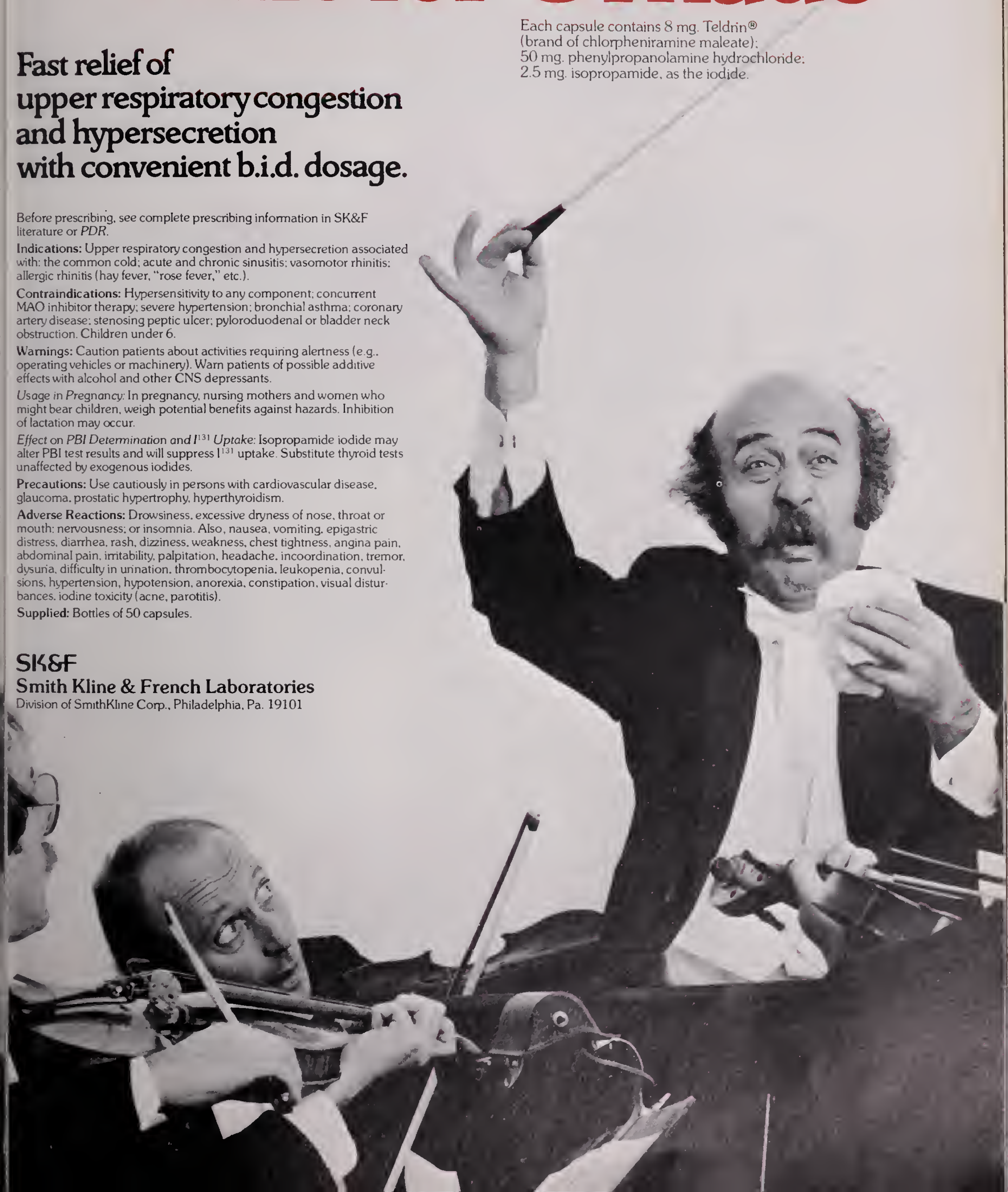

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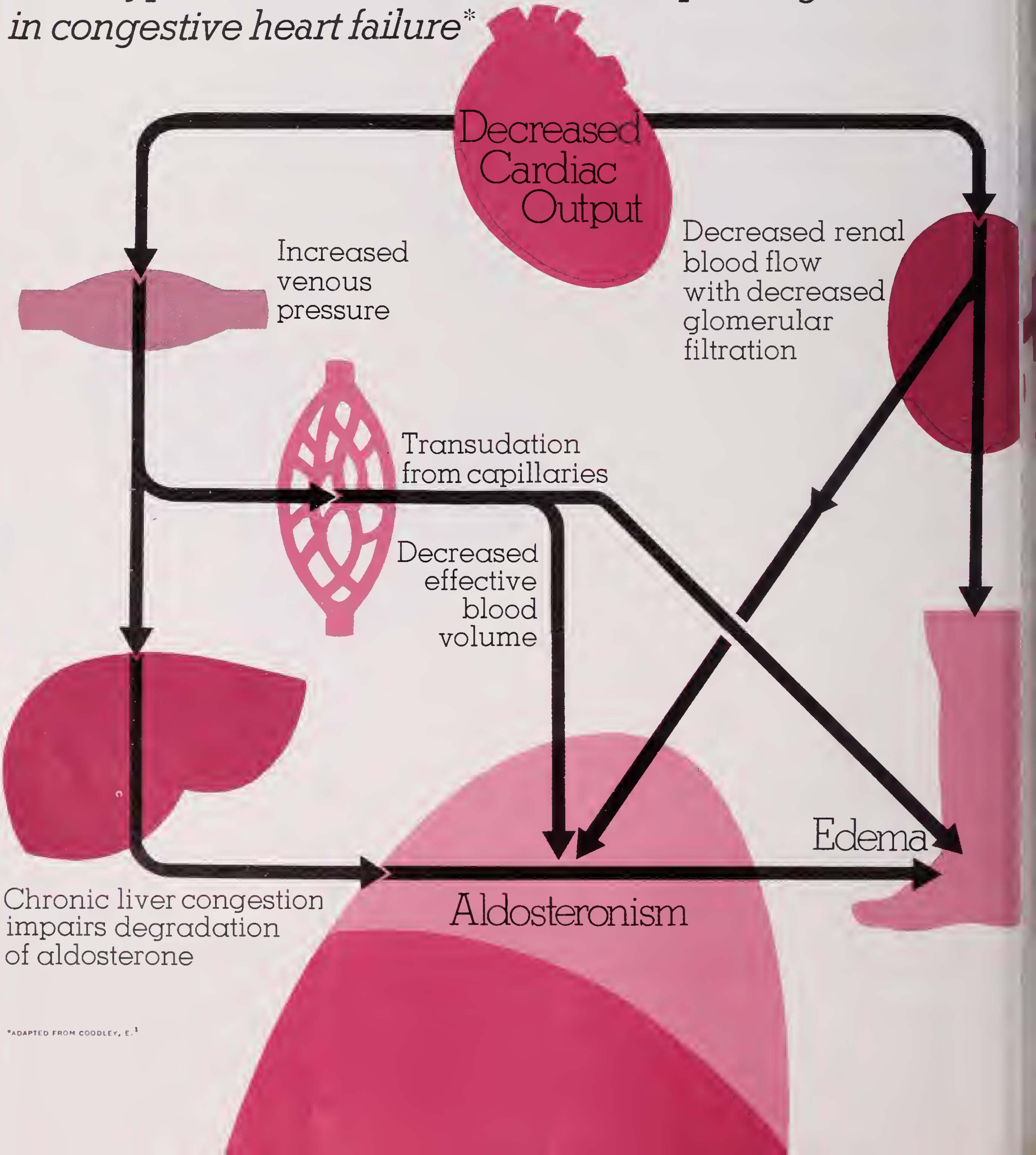

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very second or third day.
Aldactone plus "A.D.D." schedule
inimizes potassium deficiency and
otentiates effect of "add-on" diuretic.[2]
Avoids acute volume depletion and
ldosterone rebound.[2]

As a daily diuretic in combination with
daily dose of a thiazide
Permits daily additive diuretic effect
hile maintaining potassium balance.

Indications—Essential hypertension; edema or ascites of congestive heart failure, cirrhosis of the liver and the nephrotic syndrome; idiopathic edema. Some patients with malignant effusions may benefit from Aldactone (spironolactone), particularly when given with a thiazide diuretic

Contraindications—Acute renal insufficiency, rapidly progressing impairment of renal function, anuria and hyperkalemia.

Warnings—Potassium supplementation may cause hyperkalemia and is not indicated unless a glucocorticoid is also given. Discontinue potassium supplementation if hyperkalemia develops. **Usage of any drug in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the mother and fetus.**

Precautions—Patients should be checked carefully since electrolyte imbalance may occur. Although usually insignificant, hyperkalemia may be serious when renal impairment exists; deaths have occurred. Hyponatremia, manifested by dryness of the mouth, thirst, lethargy and drowsiness, together with a low serum sodium may be caused or aggravated, especially when Aldactone is combined with other diuretics. Elevation of BUN may occur, especially when pretreatment hyperazotemia exists. Mild acidosis may occur. Reduce the dosage of other antihypertensive drugs, particularly the ganglionic blocking agents, by at least 50 percent when adding Aldactone since it may potentiate their action.

Adverse Reactions—Drowsiness, lethargy, headache, diarrhea and other gastrointestinal symptoms, maculopapular or erythematous cutaneous eruptions, urticaria, mental confusion, drug fever, ataxia, gynecomastia, inability to achieve or maintain erection, mild androgenic effects, including hirsutism, irregular menses and deepening voice. Adverse reactions are infrequent and usually reversible.

Dosage and Administration—For **essential hypertension** in **adults** the daily dosage is 50 to 100 mg. in divided doses. Aldactone may be combined with a thiazide diuretic if necessary. Continue treatment for two weeks or longer since an adequate response may not occur sooner. Adjust subsequent dosage according to response of patient

For edema, ascites or **effusions** in **adults** initial daily dosage is 100 mg. in divided doses. Continue medication for at least five days to determine diuretic response; add a thiazide or organic mercurial if adequate diuretic response has not occurred. Aldactone dosage should not be changed when other therapy is added. A daily dosage of Aldactone considerably greater than 75 mg. may be given if necessary

A glucocorticoid, such as 15 to 20 mg. of prednisone daily, may be desirable for patients with extremely resistant edema which does not respond adequately to Aldactone and a conventional diuretic. Observe the usual precautions applicable to glucocorticoid therapy; supplemental potassium will usually be necessary. Such patients frequently have an associated hyponatremia—restriction of fluid intake to 1 liter per day or administration of mannitol or urea may be necessary (these measures are contraindicated in patients with uremia or severely impaired renal function). Mannitol is contraindicated in patients with congestive heart failure, and urea is contraindicated with a history or signs of hepatic coma unless the patient is receiving antibiotics orally to "sterilize" the gastrointestinal tract.

Glucocorticoids should probably be given first to patients with nephrosis since Aldactone, although useful for diuresis, will not directly affect the basic pathologic process.

For **children** the daily dosage should provide 1.5 mg. of Aldactone per pound of body weight.

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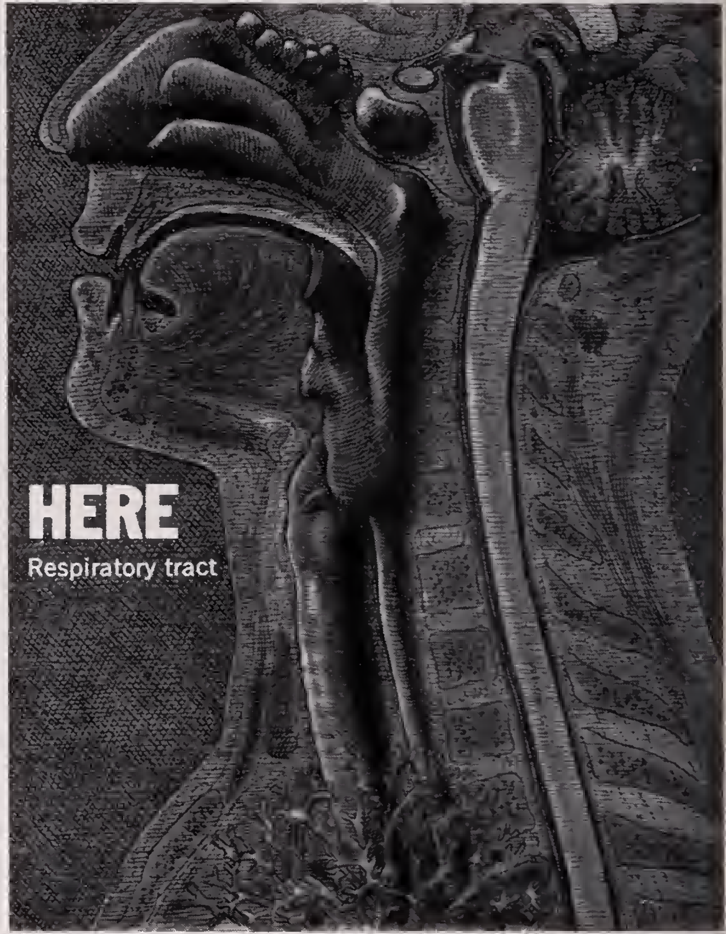

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Editorials

Exercise and Coronary Heart Disease

In this issue of Minnesota Medicine John Smith* extols the benefits derived from jogging and recommends it on a regular basis to each of us. We enjoy regular exercise and one of us (Dr. Leon) has started his second quarter century of distance running. We are very much for more physical activity for patients and for physicians, and for everyone as a part of balanced effective living, but have to question the prudence of advocating unsupervised strenuous exercise, such as jogging, for middle-aged and older people unaccustomed to physical exertion. The cardiac complications associated with strenuous exercise are real and include arrhythmias, sudden death, and myocardial infarctions.[1,2] Some myocardial damage is a common finding in animals subjected to regular strenuous exercise.[3,4] Orthopedic problems related to exercise frequently occur in middle-aged men.[5] Thus it's necessary to consider whether the risks of taking up vigorous exercise in previously sedentary middle-aged men outweigh the advantages achieved by high level physical conditioning.

The hypothesis that increased physical activity may favorably influence the incidence, age of onset, or severity of coronary heart disease (CHD) has received considerable attention during the past decade. Epidemiological studies comparing CHD incidence and mortality related to occupational and/or recreational physical activity levels have recently been critically reviewed.[6-9] Most of these studies showed an inverse relationship between the level of physical activity and CHD incidence and mortality, but physical inactivity was not found to be a risk factor of comparable magnitude to hypercholesterolemia, cigarette smoking, or hypertension. Furthermore, these types of studies do not get around the fact that individuals select themselves into jobs and habits of differing physical requirements or activity. Thus those with medical handicaps, and those without vitality and drive, the slothful, tend to select sedentary work and leisure activities. Incidentally, Dr. Smith incorrectly delegated Benjamin Franklin to this category. In actuality Franklin was an active swimmer and walker all of his life, once swimming the Thames for three and a half miles and claiming as late as age 76 (in a letter to Adams in 1782) that he was walking a "league" a day.†

Postmortem studies have failed to reveal any significant difference in the degree of coronary atherosclerosis between men whose occupations were classified as sedentary and those whose jobs were classified as physically active.[10-12] However, larger caliber coronary arteries, and less coronary occlusions and ischemic myocardial damage, were present in the hearts of heavy smokers. Experimentally, exercise training of squirrel monkeys on atherogenic diets also failed to reduce major coronary atherosclerotic changes, except for less atherosclerotic obstruction in intramyocardial arteries.[13] Therefore, it appears that increased physical activity does not prevent the main coronary atherosclerotic process. This should not be surprising since exercise does not appear to reduce substantially the principal risk factors contributing to accelerated atherogenesis, i.e., serum cholesterol levels, blood pressure and cigarette smoking. In the University of Minnesota-Penn State University collaborative study referred to by Dr. Smith, sedentary middle-aged men at relatively high CHD risk were subjected to high intensity physical activity, and no significant differences

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*See page 119.
†Personal communication from Dr. Howard B. Burchell.

in these three risk factors persisted between the control and treatment group over the 18-month training period.[14]

No objective evidence substantiates the claims of psychological benefits during chronic physical activities[15,16] though we are convinced exercise makes one feel better. Those negative findings fail to negate the positive aspects. Physiological changes associated with regular exercise which could favorably modify the course of CHD have recently been reviewed.[8,17] These include the following: (1) reduced blood coagulability and increased fibrinolysis, which could reduce the risk of coronary thrombosis, (2) demonstration in animals of improved myocardial perfusion due to increased myocardial capillary-to-fiber ratio; enlargement of coronary and collateral arteries; and increased collateral flow, and (3) metabolic and morphological changes in skeletal and cardiac muscle which result in an enhancement of cardiovascular efficiency, improved physical work capacity, and a reduction in myocardial oxygen requirements for a given work load in both healthy men and in patients with CHD. In addition, recent studies in our laboratory suggest that physical conditioning could reduce myocardial excitability[18] and increase ventricular fibrillation thresholds.[19] Physical activity clearly serves as an adjunct to dieting for control of obesity; it is truly the "secret" of weight control.

The best opportunity available to confirm the possible therapeutic value of exercise training in CHD is the proposed National Myocardial Infarction Rehabilitation Trial. Only such a collaborative study involving multiple centers can possibly answer the critical question of whether habitual high level exercise can alter the morbidity and mortality in CHD. A five-year randomized controlled study would require about 3,000 eligible survivors of myocardial infarction in order to demonstrate a significantly lower mortality rate among an experimental group receiving exercise therapy compared to a control group.[17] The recent WHO Working Group in Prague attempted to formulate an approach to an ideal secondary preventive trial involving myocardial infarct survivors. Volunteers to the secondary prevention trial would be *randomly* allocated to three treatment groups; one group would receive the best regular care available in the community; another group would enter a special care program of "multiple risk factor reduction" to include unsupervised walking as the basic physical activity—along with modification of blood pressure and dietary and smoking habits as required; and a third group would be offered the same special care multifactor hygienic regimen *plus* a supervised program of intensive exercise aimed at securing high levels of cardiovascular conditioning.

While waiting for definitive evidence about the benefits of exercise in CHD what then can the practitioner prescribe in terms of physical activity for middle-aged, coronary-prone men or myocardial infarction survivors? Based on current knowledge, increased physical activity should be presented as part of a balanced hygienic program to include elimination of cigarette smoking, a diet lower in saturated fats and calories, and control of elevated blood pressure when applicable. The type and amount of physical activity should be prescribed on an individualized basis depending on the results of periodic evaluation of physiological capacity and cardiovascular reserve with consideration of the patient's desires skills and values. Progressive exercise stress testing is, in the absence of contraindications, the best method of assessing exercise capacity and formulating an exercise prescription. In general, regular walking to tolerance, i.e., to a point *short* of exhaustion, marked dyspnea or chest pain, is the safest unsupervised exercise to prescribe as part of any hygienic program and as the initial level of a more intensive progressive exercise training program.

If a progressive conditioning program is desired by the physician and patient and there are no obvious contraindications, level of endurance exercise can be advanced by increasing the rate and distance of walking, or by prescribing other large muscle isotonic activity such as walking-jogging, swimming, cycling, calisthenics, or other non-competitive recreational activities to be performed at a pulse rate below the level successfully negotiated on stress testing in the office. Preferably the exercise should be carried out under supervised conditions. Five to ten minute warm-up and cool-down periods should be included (rather than Smith's last minute sprint up the driveway to impress the neighbors). Three or four sessions a week of endurance training for 30 to 60 minute periods achieve substantial physical training effects, which can be maintained by two such sessions weekly.[8,21] Individuals with evidence of CHD and those at high risk should be advised to avoid competitive activity, sudden bursts of effort, isometric exercises including static work such as lifting, shoveling, or painting with arms elevated. Calisthenics which severely stress the low back and knees are also contraindicated. Subjects who fail to show significant conditioning effects after three months of exercise training will probably not benefit from exercise.

Although we think that jogging shouldn't be recommended for everyone, it is clear that regular physical activity as part of a hygienic life style plays a role in maintaining an efficient cardiovascular system and "a sound mind in a sound body." Well-designed and controlled studies are sorely needed to determine if conditioning exercise will reduce the morbidity and mortality associated with CHD; such studies should be actively supported by the medical profession rather than adopting either nihilistic or overly enthusiastic attitudes toward exercise.

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More Time with the Patient

THERE IS A TENDENCY for the students and the house staff to present the initial workup of their patients to the attending physician in teaching hospitals, not at bedside, but in the corridor, hall, or the conference room. This is in contrast to the traditional bedside presentation of the history with further questioning by the attending and with participation of the patient who provided additional details and clarification. Then the clinical findings were described and verified by the attending who pointed out missed or misinterpreted signs. Subsequently, diagnostic possibilities were considered, the proposed roentgenologic and laboratory studies were evaluated and therapeutic management was discussed or initiated. Tact, respect, discretion, empathy and sympathy guided the bedside discussion of the potential diagnoses, management, and prognosis.

The patients, as a rule, appreciated these deliberations and valued the thoughtful considerations in regard to their disrupted well being. They became aware of a planned sequence of action to establish the diagnosis, and they realized the time and effort spent on their behalf. The patients also appreciated the recognition of their rights to be informed of the purpose and justification of the various tests and examinations, the diagnostic considerations, the therapeutic decisions, and prognostic expectations. The various studies appeared as part of a plan for sequential approach where after the results of the first tests were obtained, then subsequent tests would be considered and requested. The description of planned examinations relieved part of the anxiety associated with the diagnostic workup and prepared the patient for the various tests.

During the bedside presentation, the medical students had an opportunity to observe a seasoned clinician establish rapport and communicate with the patient, elicit additional pertinent information and perform part or the entire physical examination in the traditional way. The students reflected on the significance of clinical experience and appreciated the art of medicine and the value of the warmth and friendliness in the physician's personality. By observing their teachers they gradually recognized the importance and the meaning of the initial visit and the daily rounds, and developed good clinical habits.

Now, when "the case" is presented away from the bedside and subsequently the attending physician steps into the room briefly for a superficial communication with the patient, the students gradually underrate the value of the doctor's visit; they underestimate the significance of the interpersonal rapport and communication with the patient. When they see their clinical instructor approach "the case" in an impersonal way, they start believing that this is the acceptable, proper and workable way. They cannot correct this impression in their wards by observing the intern or resident because, themselves too, at that stage of their training and practice of medicine have a tendency to be more disease than patient oriented.

Not only the initial presentation but also the daily follow-up visits in teaching hospitals are conducted more and more outside the patient's room. They become more or less chart rounds with most of the time spent in discussion of abnormal laboratory findings and their significance. Subsequently, there is a brief visit with the patient which becomes an anticlimax after the exciting discussion of "the case." The patient usually is given verdicts and very little time is allocated for him to ask questions or express any feelings or any thoughts.

Consequently, the medical student gets a distorted picture of the purpose, the function and the importance of the daily doctor visits, and he/she carries this impression later in his/her office and hospital practice of medicine.

Although, today the physician receives more help in patient care from paramedical personnel, social workers, psychologists, dieticians, occupational and physical therapists, etc. he is still responsible for the coordination of their activities and he provides the continuity in the care of the patient. For this reason, his visits remain of paramount importance to the patient.

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Emergency Room Experience with Chemical Abuse

THE DRUG ABUSE SECTION of the State Planning Agency authorized Pearson and Steger to prepare a survey of alcohol and other drug related incidents in Minnesota.* A continuous 10-day census of Emergency Rooms was used. Hospital staffs throughout the state supplied the raw data. Visits were tabulated by day of week, sex, age, description of the incident, and identification of all psychoactive substances known or believed to be in the patient's system. Immediate dispositions were classified as discharged, hospitalized, referred, or deceased. Exactly 500 incidents were reported. This represents approximately 5% of all Emergency Room admissions to participating hospitals. Table 1 summarizes findings by percentage.

Table 2 displays the age and sex distribution of the patient. Table 3 shows drug incidents reported as ingestions, overdose or unconsciousness. Table 4 displays alcohol related vehicular accidents.

The salient findings in this study are as follows: (1) 67% involved males, 33% involved females with alcohol incidents accounting for the higher ratio of males. (2) Persons under 25 account for 49% of all incidents. 71% of the cases are in patients under the age of 35. (3) Single and multiple drug incidents requiring attention were usually due to the effect of the drug itself. 90% of these were reported as ingestions, overdose or unconsciousness. Alcohol

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*Unpublished data.

TABLE 1

Hospital Survey*

Alcohol and Other Drug Related Incidents In Minnesota During The Spring of 1973

Area Board	Sex		Chemical			Dispositions		
	M	F	Alcohol	Other Drug	Drug Combination†	Dis-charged	Hos-pitalized	Referral
Anoka	77%	23%	70%	17%	13%	83%	6%	11%
Carver-Scott	90%	10%	64%	36%	—	55%	45%	—
Central Minnesota	75%	25%	40%	60%	—	34%	50%	16%
Dakota	47%	53%	70%	18%	12%	53%	35%	12%
Duluth	79%	21%	71%	14%	15%	46%	42%	8%
Five County	61%	39%	46%	39%	15%	54%	38%	8%
Hennepin	56%	44%	51%	35%	14%	40%	38%	21%
Hiawatha Valley	40%	60%	60%	20%	20%	20%	80%	—
Lakeland	74%	26%	58%	26%	16%	41%	59%	—
Minnesota Valley	78%	22%	78%	11%	11%	89%	11%	—
Mower County	67%	33%	78%	11%	11%	66%	34%	—
Northland	83%	17%	88%	6%	6%	72%	28%	—
Northern Pines	57%	43%	48%	33%	19%	52%	48%	—
Northwestern	62%	38%	54%	23%	23%	30%	52%	—
St. Paul-Ramsey	49%	51%	44%	40%	16%	67%	30%	3%
Range	62%	38%	82%	6%	12%	43%	37%	13%
Sioux Trails	84%	16%	100%	—	—	46%	39%	15
Southern Minnesota	71%	29%	42%	58%	—	—	100%	—
Southwestern	70%	30%	70%	15%	15%	70%	30%	—
Upper Mississippi	60%	40%	70%	10%	20%	60%	30%	10%
Washington County	62%	38%	75%	25%	—	37½%	50%	12½%
West Central	80%	20%	73%	27%	—	60%	40%	—
Western	62%	38%	50%	38%	12%	62%	12%	26%
Luther Youngdahl	72%	28%	82%	9%	9%	45%	45%	10%
Zumbro Valley	62%	38%	67%	19%	14%	62%	28%	10%
Median	67%	33%	70%	20%	12%	53%	38%	8%

* Seventy-five percent (75%) of the hospitals responded to the questionnaire

† Any combination of two or more chemicals.

TABLE 2

Age and Sex

All Incidents Involving Mood Altering Chemicals

Age	Males	Females	Total	Cumulative %
0-9	24	14	38	8%
10-13	3	1	4	8%
14-17	30	37	67	22%
18-24	99	37	136	49%
25-34	73	37	110	71%
35-44	38	15	53	82%
45-60	48	21	69	95%
61+	18	5	23	100%
Totals:	333	167	500	

TABLE 3

Drug and Drug Combination Incidents

Reported as Ingestion, Overdose, or Unconsciousness

(90% Of All Drug and Drug Combination Incidents)

Age	Males	Females	Total	Cumulative %
0-9	24	12	36	20%
10-13	3	1	4	22%
14-17	17	27	44	47%
18-24	26	19	45	72%
25-34	7	20	27	87%
35-44	5	4	9	92%
45-60	6	7	13	99%
61+	....	1	1	100%
Totals:	88	91	179	

TABLE 4

Alcohol Related Vehicle Accidents

(32% Of All Alcohol Incidents)

Age	Males	Females	Total	Cumulative %
0-9	....	1	1	1%
10-13	....	....	....	....
14-17	4	5	9	10%
18-24	33	9	42	54%
25-34	22	2	24	78%
35-44	5	2	7	86%
45-60	5	1	6	92%
61+	6	2	8	100%
Totals:	75	22	97	

incidents were connected with vehicular accidents in 32% or other trauma in 32%. (5) The bulk of all non-alcohol incidents were involved with legal or prescription type chemicals. Only 6% involved an illegal substance. (6) Most chemically related Emergency Room admissions occur with chemicals that people think of as being either a social beverage, a sedative, or a tranquilizer.

This illuminating home-grown study should aid practicing physicians and medical educators in several ways. Though the study was not intended to determine the quality of care rendered emergently and in followup, it points to the need for thorough training in the area of substance abuse related illness and trauma. A diagnosis of chronic chemical abuse can and should be made and acted upon at the Emergency Room level.

Access to subacute and chronic care facilities must be easy and fast. Often a patient's willingness to enter treatment is greatest shortly after an acute episode requiring medical attention.

In view of the percentage total admissions these incidents represent, it is clear that formal and mandatory training in this area is required of all health care workers. It is noteworthy that not a single required hour of clinical teaching in substance abuse is given at the University of Minnesota Medical School.

Robert Maslansky, M.D.
Minneapolis, Minnesota

Letters to the Editor

Dear Editor:

I read with interest the article by Suros and Lee* in the September issue, entitled, "Pneumoretroperitoneum, Pneumomediastinum and Subcutaneous Emphysema." I would appreciate your inquiring of the authors the following, which I think are of considerable interest. What were the results of microbiologic studies prior to antibiotic therapy and at the time of surgical intervention in the two cases? The role of aerobic versus anaerobic enteric organisms would be of particular interest. What was the nature of the "air" (? gas) in case one, i.e., was the gas or perhaps mixture of gases foul smelling suggesting H_2S production and possibility of anaerobic infection. This information would help us better understand some of the problems as to the derivation, type and meaning of gas in tissues. This, in turn, would facilitate making decisions regarding an understandable empiric use of antibiotics. The term the authors used "broad-spectrum antibiotic" becomes ambiguous if not a misnomer, with our current understanding of the role of aerobes and anaerobes and their respective antibiotic sensitivities.

Robert P. Gruninger, M.D.,
Director—Division of Infectious Diseases,
Saint Vincent Hospital, Worcester, Massachusetts

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*Suros Juan and Lee RA: Pneumoretroperitoneum, pneumomediastinum and subcutaneous emphysema. Minnesota Med 56:745, 1973.

References

Finegold SM and Rosenblatt JE: Medicine, 52, 311, 1973.
MacLennan JD: Bact. Reviews, 26, 177, 1962.

Dear Editor:

In response to Dr. Robert P. Gruninger's letter the culture of the fluid material taken from the first patient at surgery failed to grow anaerobic organisms. The culture from the second patient grew *Escherichia coli* and had the following antibiotic sensitivity: cephalothin 10, ampicillin 5, streptomycin 5, tetracycline 5, kanamycin 5, polymyxin group 5, and gentamicin 1. The patient was started on therapy with chloramphenicol, gentamicin, and penicillin at the time of operation, which accounts for our use of the term "broad spectrum antibiotic coverage." The gas released from the abdominal cavity at operation had no odor.

Raymond A. Lee, M.D.
Mayo Clinic and Mayo Foundation
Rochester, Minnesota

Minnesota State Medical Association

121st Annual Meeting of the Minnesota State Medical Association will be held in Duluth, May 16 and 17, in the Duluth Arena-Auditorium.

Letters to the Editor (continued)

The Greenback Poultice*

Dear Editor:

Are we in the age of litigation? From time immemorial man has endeavored to blame someone for his own stupidity as well as for circumstances beyond the specific control of anyone.

Within our memories of the past, our ancestors settled their anger-producing differences with fisticuffs and duels. This seemed too rough and often fatal, and so laws were passed making battery and dueling illegal.

In my childhood with Dad we were leaving the Sisseton Indian Reservation pow-wow in a long line of vehicles. It was necessary to cross over a barbed wire fence which was being held down in order that the teams with wagons and buggies and an occasional car with pneumatic tires (rubber tires were not so sturdy in those days) could get out of the enclosure. In order to avoid the barbed wire, Dad, proudly driving his newly-purchased Overland, accidentally ran into the rear end of a horse and buggy outfit. The minor impact alarmed the driver and startled the team, but caused no physical damage. A few harsh words were spoken for a moment, but Dad, realizing his error, pulled out his pocket money pouch, tendered the man four large† green one dollar bills, a handful of small change, and suggested that the man stop in and see the doctor on his way home to be certain that he had not been injured. That seemed like a generous settlement and no further remarks were made or needed. The man visited the small town doctor who made a cursory examination, found no evidence of injury in the back, applied a prophylactic, psychosomatic aromatic mixture of tincture of arnica and balsam peru, and suggested that the man use a flaxseed poultice if he should develop any discomfort.

Nowadays that rear-end collision would have been settled more legally with witnesses and doctors, and lawyers who might compound an analogous incident into a horrifying whiplash injury and maintain in a $50,000 Summons that it was the cause of all manner of aches and pains before, after, and in the future. A damage of $150 to a fender might be referred to as having been "totaled out," and a simple strain of the neck might call forth a host of consultants, extensive laboratory tests, Xrays, electroencephalograms, electromyograms, a hospital stay and a six weeks course of hot packs and physiotherapy. The individual might even develop iatrogenic as well as liticogenic symptoms.

Tincture of arnica, balsam peru, and flaxseed cataplasm might serve just as well, but only a generous greenback poultice could assure one of immediate benefits.

Carl O. Rice, M.D., Ph.D.
Editor Emeritus

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*Netter MD: Ciba Clin. Symposium 25:3, 1973.

†7.42 x 3.13 inches prior to 1929 vs 6.14 x 2.61 inches now, green on the back side, grey on the front.

Dear Editor:

The article, Ophthalmia Neonatorum, by Boone et al.* is timely and important in light of the current incidence of venereal disease. The table comparing onset periods is especially helpful in distinguishing between chemically induced conjunctivitis and infectious conditions due to the gonococcus.

There is one misleading statement in the section headed "Epidemiology" which should not be allowed to pass. The initial sentence reads "Since this is not a reportable disease, the exact incidence of ophthalmia neonatorum is not known."

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*Boone WB, Doughman LJ and Harris JE: 56:940, 1973.

Letters to the Editor (continued)

Besides being a non sequitur, this is not true. State Board of Health regulations from the dear dead days of pre-antibiotic antiquity include both "Ophthalmia Neonatorum" and "Conjunctivitis, epidemic" as conditions to be reported by the attending physician wthin 24 hours of being called to such a case; when no physician is in attendance it shall be the duty of the head of the household or other persons in charge to report immediately.

Of course, even though the disease is reportable, the exact incidence may not be known. Reported cases of ophthalmia neonatorum in Minnesota in recent years are shown as follows:

Year	Number	Year	Number	Year	Number
1958	0	1963	2	1968	0
1959	0	1964	1	1969	0
1960	2	1965	0	1970	2
1961	0	1966	0	1971	0
1962	1	1967	0	1972	1

D. S. Fleming, M.D.
Director
Division of Personal Health Services

Dear Editor:

In the December issue of MINNESOTA MEDICINE a letter appears by Leonore Kaplan,* a social worker. In this letter she complains about a physician stating that a patient could work at a job where she "sat down" and implying that the physician failed to use judgment and common sense.

There are very few people who are totally and completely disabled. Most people have disabilities which prevent them from doing certain types of work. In the forms that are supplied to us by Social Security and other organizations they usually ask for information as to what the person can and cannot do. It is the responsibility of the physician to answer the questions truthfully, and not to interpret the law.

If the purpose of the law was to provide income for the patients in question, then it should be carried out that way. If the Social Security Administration is not following the *purpose* in this regard, then appeals should be made to them to follow the purpose of the law. It is unfair to ask the physician to falsify the statement so a patient can get money from this or that governmental agency.

If Mrs. Kaplan has objections, it properly should be to the way the law was written and not to the physician who is just trying to follow the instructions given to him by the agency involved. In the case mentioned it might be possible that the patient referred to could carry out simple assembly line procedures in a sitting position. If the patient *could* do such work, but was unable to perform the work because such work was not available in the area, that is a social and not a medical problem and should be attacked by trying to get the law or the regulation changed, not by jumping on doctors. Let's pass the responsibility to where it belongs, to poorly drawn laws.

Erick Reeber, M.D.
Bagley, Minnesota

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*See page 1057.

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AN IMPORTANT NOTE:
It has not been established whether the drug-induced lowering of serum cholesterol or lipid levels has a detrimental, beneficial, or no effect on the morbidity or mortality due to atherosclerosis or coronary heart disease. Several years will be required before current investigations will yield an answer to this question.

CHOLOXIN® (sodium dextrothyroxine) Single-Tablet-A-Day Dosage Schedules

See prescribing information in package insert reproduced below.

	Starting Dosage	Increased by Increments of	Usual Maintenance	Maximal Recommended
Adult Hypercholesterolemic	1.0-2.0 mg.	monthly 1.0-2.0 mg.	4.0-8.0 mg.	4.0-8.0 mg.
Pediatric Hypercholesterolemic	0.05 mg./kg. body weight	monthly 0.05 mg./kg.	0.1 mg./kg. body weight	4.0 mg.
Hypothyroid Cardiac Patients	0.5-1.0 mg.	monthly 1.0 mg.	4.0 mg.	4.0 mg.

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Description
CHOLOXIN (sodium dextrothyroxine) is the sodium salt of the dextrorotatory isomer of thyroxine. It is chemically described as D-3,5,3′,5′-tetraiodothyronine sodium salt.

Actions
The predominant effect of CHOLOXIN (sodium dextrothyroxine) is the reduction of serum cholesterol levels in hyperlipidemic patients. Beta lipoprotein and triglyceride fractions may also be reduced from previously elevated levels.

Most of the available evidence indicates that CHOLOXIN stimulates the liver to increase catabolism and excretion of cholesterol and its degradation products via the biliary route into the feces. Cholesterol synthesis is not inhibited and abnormal metabolic end-products do not accumulate in the blood.

Indications
This is not an innocuous drug. Strict attention should be paid to the indications and contraindications.

CHOLOXIN (sodium dextrothyroxine) is an antilipidemic agent used as an adjunct to diet and other measures for the reduction of elevated serum cholesterol (low density lipoproteins) in euthyroid patients with no known evidence of organic heart disease.

The drug is also indicated in the treatment of hypothyroidism in patients with cardiac disease who cannot tolerate other types of thyroid medication.

Before prescribing, note the following: Results from a randomized clinical study have indicated a possible adverse effect when CHOLOXIN is administered to a patient receiving a digitalis preparation. There may be an additive effect. This additive effect may possibly stimulate the myocardium excessively in patients with significant myocardial impairment. CHOLOXIN dosage should not exceed 4 mg per day when the patient is receiving a digitalis preparation concomitantly. Careful monitoring of the total effect of both drugs is important.

It has not been established whether the drug-induced lowering of serum cholesterol or lipid levels has a detrimental, beneficial, or no effect on the morbidity or mortality due to atherosclerosis or coronary heart disease. Several years will be required before current investigations will yield an answer to this question.

Contraindications
The administration of CHOLOXIN (sodium dextrothyroxine) to euthyroid patients with one or more of the following conditions is contraindicated:

1. Known organic heart disease, including angina pectoris; history of myocardial infarction; cardiac arrhythmia or tachycardia, either active or in patients with demonstrated propensity for arrhythmias; rheumatic heart disease; history of congestive heart failure; and decompensated or borderline compensated cardiac status.
2. Hypertensive states (other than mild, labile systolic hypertension).
3. Advanced liver or kidney disease.
4. Pregnancy.
5. Nursing mothers.
6. History of iodism.

Warnings
CHOLOXIN (sodium dextrothyroxine) may potentiate the effects of anticoagulants on prothrombin time. Reductions of anticoagulant dosage by as much as 30% have been required in some patients. Consequently, the dosage of anticoagulants should be reduced by one-third upon initiation of CHOLOXIN therapy and the dosage subsequently readjusted on the basis of prothrombin time. The prothrombin time of patients receiving anticoagulant therapy concomitantly with CHOLOXIN therapy should be observed as frequently as necessary, but at least weekly, during the first few weeks of treatment.

In the surgical patient, it is wise to consider withdrawal of the drug two weeks prior to surgery if the use of anticoagulants during surgery is contemplated.

When CHOLOXIN is used as thyroid replacement therapy in hypothyroid patients with concomitant coronary artery disease (especially those with a history of angina pectoris or myocardial infarction) or other cardiac disease, treatment should be initiated with care. Special consideration of the dosage schedule of CHOLOXIN is required. This drug may increase the oxygen requirements of the myocardium, especially at high dosage levels. Treated subjects with coronary artery disease must be seen at frequent intervals. If aggravation of angina or increased myocardial ischemia, cardiac failure, or clinically significant arrhythmia develops during the treatment of hypothyroid patients, the dosage should be reduced or the drug discontinued.

Special consideration must be given to the dosage of other thyroid medications used concomitantly with CHOLOXIN. As with all thyroactive drugs, hypothyroid patients are more sensitive to a given dose of CHOLOXIN than euthyroid patients.

Epinephrine injection in patients with coronary artery disease may precipitate an episode of coronary insufficiency. This condition may be enhanced in patients receiving thyroid analogues. These phenomena should be kept in mind when catecholamine injections are required in sodium dextrothyroxine-treated patients with coronary artery disease.

Since the possibility of precipitating cardiac arrhythmias during surgery may be greater in patients treated with thyroid hormones, it may be wise to discontinue CHOLOXIN in euthyroid patients at least two weeks prior to an elective operation. During emergency surgery in euthyroid patients, and in surgery in hypothyroid patients in whom it may be advisable to withdraw therapy, the patients should be carefully observed.

There are reports that sodium dextrothyroxine in diabetic patients is capable of increasing blood sugar levels with a resultant increase in requirements of insulin or oral hypoglycemic agents. Special attention should be paid to parameters necessary for good control of the diabetic state in dextrothyroxine-treated subjects and to dosage requirements of insulin or other antidiabetic drugs. If sodium dextrothyroxine is later withdrawn from patients who had required an increase of insulin (or oral hypoglycemic agents) dosage during its administration, the dosage of antidiabetic drugs should be reduced and adjusted to maintain good control of the diabetic state.

When either or both impaired liver or kidney function are present, the advantages of CHOLOXIN therapy must be weighed against the possibility of deleterious results.

Usage in Women of Childbearing Age
Women of childbearing age with familial hypercholesterolemia or hyperlipemia should not be deprived of the use of this drug; it can be given to those patients exercising strict birth control procedures. Since pregnancy may occur despite the use of birth control procedures, administration of CHOLOXIN (sodium dextrothyroxine) to women of this age group should be undertaken only after weighing the possible risk to the fetus against the possible benefits to the mother. Teratogenic studies in two animal species have resulted in no abnormalities in the offspring.

Precautions
It is expected that patients on dextrothyroxine therapy will show greatly increased serum protein-bound-iodine levels. These increased serum PBI values are evidence of absorption and transport of the drug, and should NOT be interpreted as evidence of hypermetabolism; similarly, they may not be used for titrating the effective dose of CHOLOXIN (sodium dextrothyroxine). PBI values in the range of 10 to 25 mcg% in treated patients are common.

If signs or symptoms of iodism develop during CHOLOXIN therapy, the drug should be discontinued.

A few children with familial hypercholesterolemia have been treated with CHOLOXIN for periods of one year or longer with no adverse effects on growth. However, it is recommended that the drug be continued in patients in this age group only if a significant serum cholesterol-lowering effect is observed.

Adverse Reactions
The side effects attributed to dextrothyroxine therapy are, for the most part, due to increased metabolism, and may be minimized by following the recommended dosage schedule. Adverse effects are least commonly seen in euthyroid patients with no signs or symptoms of organic heart disease; the incidence of adverse effects is increased in hypothyroid patients, and is highest in those patients with organic heart disease superimposed on the hypothyroid state.

In the absence of known organic heart disease, some cardiac changes may be precipitated during sodium dextrothyroxine therapy. In addition to angina pectoris, arrhythmia consisting of extrasystoles, ectopic beats, or supraventricular tachycardia, ECG evidence of ischemic myocardial changes and increase in heart size have been observed. Myocardial infarctions, both fatal and non-fatal, have occurred, but these are not unexpected in untreated patients in the age groups studied. It is not known whether any of these infarcts were drug related.

Changes in clinical status that may be related to the metabolic action of the drug include the development of insomnia, nervousness, palpitations, tremors, loss of weight, lid lag, sweating, flushing, hyperthermia, hair loss, diuresis, and menstrual irregularities. Gastrointestinal complaints during therapy have included dyspepsia, nausea and vomiting, constipation, diarrhea, and decrease in appetite.

Other side effects reported to be associated with CHOLOXIN (sodium dextrothyroxine) therapy include the development of headache, changes in libido (increase or decrease), hoarseness, tinnitus, dizziness, peripheral edema, malaise, tiredness, visual disturbances, psychic changes, paresthesia, muscle pain, and various bizarre subjective complaints. Skin rashes, including a few which appeared to be due to iodism, and itching have been attributed to dextrothyroxine by some investigators. Gallstones have been discovered in occasional dextrothyroxine-treated patients and cholestatic jaundice has occurred in one patient, although its relationship to CHOLOXIN therapy was not established.

In several instances, the previously existing conditions of the patient appeared to continue or progress during the administration of CHOLOXIN; a worsening of peripheral vascular disease, sensorium, exophthalmos, and retinopathy have been reported.

CHOLOXIN potentiates the effects of anticoagulants, such as warfarin or Dicumarol, on prothrombin time, thus indicating a decrease in the dosage requirements of the anticoagulants. On the other hand, dosage requirements of antidiabetic drugs have been reported to be increased during dextrothyroxine therapy (see WARNINGS section).

Dosage and Administration
For **adult** euthyroid hypercholesterolemic patients, the recommended maintenance dose of CHOLOXIN (sodium dextrothyroxine) is 4 to 8 mg per day. The initial daily dose should be 1 to 2 mg to be increased in 1 to 2 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily, if that dosage level is indicated to effect the desired lowering of serum cholesterol.

When used as partial or complete substitution therapy for levothyroxine in hypothyroid patients with cardiac disease who cannot tolerate other types of thyroid medication, the initial daily dose should be 1 mg to be increased in 1 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily, preferably the lower dosage. The maximum in patients receiving digitalis therapy is 4 mg.

For **pediatric** hypercholesterolemic patients, the recommended maintenance dose of CHOLOXIN is approximately 0.1 mg per kilogram. The initial daily dosage should be approximately 0.05 mg per kilogram to be increased in up to 0.05 mg per kilogram increments at monthly intervals. The recommended maximal dose is 4 mg daily, if that dosage is indicated to effect the desired lowering of serum cholesterol.

If new signs or symptoms of cardiac disease develop during the treatment period, the drug should be withdrawn.

How Supplied
CHOLOXIN (sodium dextrothyroxine) is supplied in prescription packages of scored 1, 2, 4, and 6 mg tablets.

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X-Ray Conference

Aortic Arch Anomaly in an Asymptomatic Child

A five-year-old girl was being evaluated for a condition totally unrelated to the roentgenogram shown below (Figure 1). A routine chest film was obtained although the child had no symptoms referrable to the chest.

What is your diagnosis?

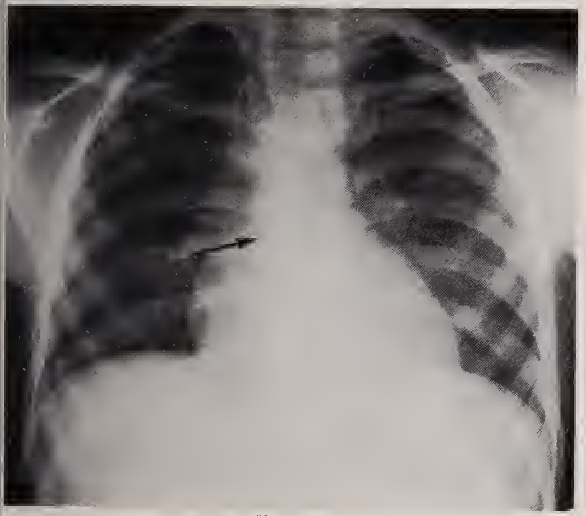

Figure 1

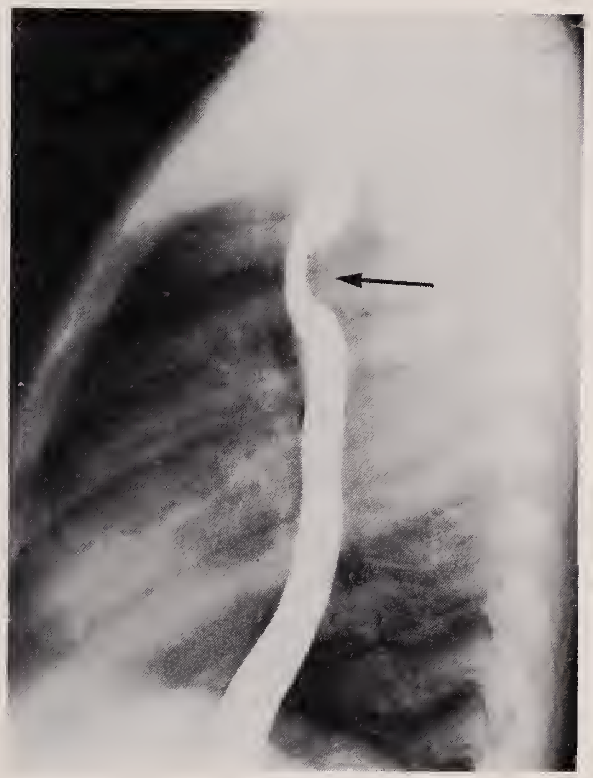

Figure 2

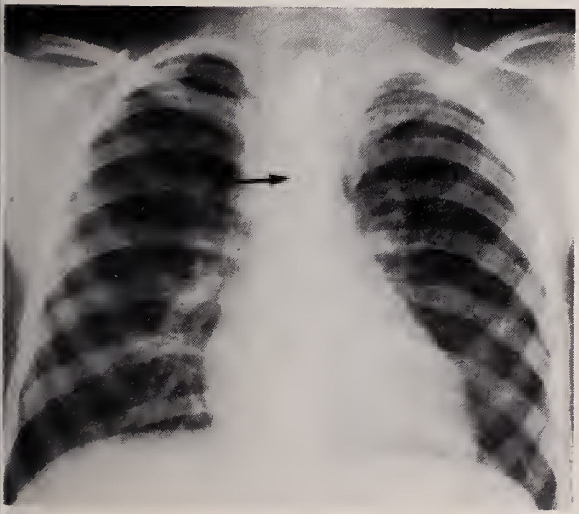

Figure 3

Diagnosis: Right aortic arch with aberrant left subclavian artery, left ductus arteriosus, and right descending aorta.

The right aortic arch and right descending aorta can be seen on the routine chest film (arrows, Figure 1). A barium esophagram shows a large retroesophageal filling defect on the lateral view (arrow, Figure 2) which is caused by the bulbous origin of the aberrant left subclavian artery, the arch of the aorta, and the upper portion of the descending aorta. A similar, almost indistinguishable retroesophageal defect can be seen in cases of double aortic arch. On the PA view a right-sided esophageal filling defect can be seen (arrow, Figure 3) which represents the impression of the right aortic arch.

There are three major subgroups of right aortic arch, named according to the type of vascular branching:[2] (1) Mirror image branching, (2) aberrant left subclavian artery, and (3) isolation of the left subclavian artery from the aorta. Right aortic arch with aberrant left subclavian artery is the most common variety of right aortic arch and is usually associated with a left ductus arteriosus, although a small percentage are associated with a right ductus arteriosus. The order in which the vessels arise from right aortic arch with aberrant left subclavian is left common carotid, right common carotid, right subclavian, and left subclavian arteries (Figure 4).

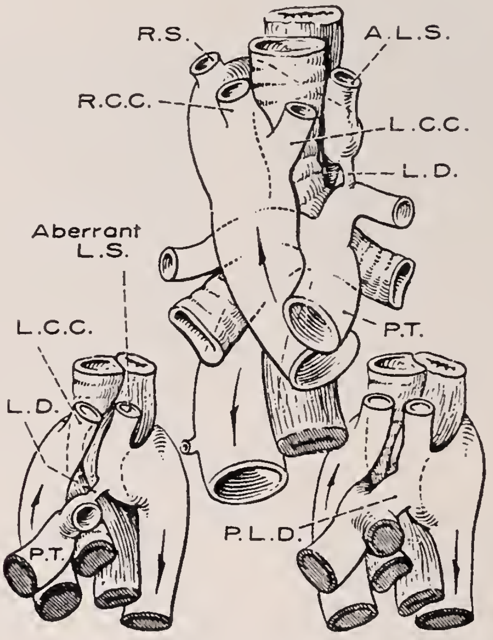

Fig. 4. The main illustration views the malformation from the front. The two smaller drawings, which are left lateral views, illustrate the presence of a nonpatent and a patent left ductus arteriosus. The trachea and esophagus are completely encircled by the pulmonary artery and ascending aorta anteriorly, the right arch on the right, the junction of the right arch, left dorsal aortic root, and upper descending aorta posteriorly, and the left dorsal aortic root and left ductus arteriosus on the left. (From: An Atlas of Vascular Rings and Related Malformations of the Aortic Arch System 1964, by J. R. Stewart, W. Kincaid, and J. E. Edwards; with permission of Charles C. Thomas, Publisher and J. R. Stewart M.D., San Antonio, author. A.L.S. aberrant left subclavian artery; L.C.C. left common carotid a.; L.D. left ductus arteriosus; R.C.C. right common carotid a.; R.S. right subclavian a.; P.T. pulmonary trunk; P.L.D. patent left ductus arteriosus.

Right aortic arch with mirror image branching is reported more frequently than a right arch with aberrant left subclavian artery in some series because it has a high correlation with congenital heart disease and these individuals seek medical attention more frequently than do those persons with aberrant left subclavian artery who are usually asymptomatic. In a large series at the Mayo Clinic,[3] approximately 60% of right aortic arches were associated with mirror image branching, about 40% were associated with aberrant left subclavian artery, and a small fraction were associated with isolation of the left subclavian artery from the aorta. In those patients with mirror image branching, 98% had congenital heart disease and 2% had normal hearts, while in those with aberrant left subclavian artery only 12% had congenital heart disease and 88% had normal hearts. It was the impression of Stewart et al.[3] that their series was spuriously weighted in favor of right aortic arch with mirror-image branching because many patients had been referred for correction of congenital heart disease.

Summary

Patients with right aortic arch with aberrant left subclavian artery can usually be diagnosed by barium esophagram. No further work-up is necessary unless the patient has evidence of congenital heart disease or symptoms of tracheal or esophageal compression.

Rudy G. Thell
Medical Student
University of Minnesota

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2. Stewart JR, Kincaid OW and Edwards JE: An Atlas of Vascular Rings and Related Malformations of the Aortic Arch System. Charles C. Thomas. Publisher, Springfield, Illinois, 1964.
3. Stewart JR, Kincaid OW and Titus JL: Right aortic arch: plain film diagnosis and significance. Amer J Roentgenol 97:377, 1966.

Dr. Russell V. Lucas, Jr.

Dr. Russell V. Lucas, Jr., is the newly-appointed Director of the Electrocardiology Laboratory at Children's Hospital, St. Paul. He will be able to read children's electrocardiograms through the telephone wires between the St. Paul Hospital and his office in Minneapolis, if he needs to do so.

Dr. Lucas, who is a Professor in Pediatric Cardiology at the University of Minnesota, divides his time between the Children's Hospital and the University of Minnesota each week.

No signs of violence were to be discovered upon Sir Charles's person, and though the doctor's evidence pointed to an almost incredible facial distortion—so great that Dr. Mortimer refused at first to believe that it was indeed his friend and patient who lay before him—it was explained that that is a symptom which is not unusual in cases of dyspnoea and death from cardiac exhaustion. This explanation was borne out by the post-mortem examination, which showed long-standing organic disease, and the coroner's jury returned a verdict in accordance with the medical evidence.*

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*Arthur Conan Doyle: The Hound of the Baskervilles, Chap. II. 1901.

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Run for Your Wife

JOHN E. SMITH, M.D.*

THE TITLE IS NOT a typographical error, and I don't have a speech impediment. But there is a growing body of hearsay that athletes are "sexier" than non-athletes. By inference this is also true of the part-time athlete, and by further extension even to the guy who just works out once in awhile.

Matter of Good Health

It's simply a fundamental matter of good health. The healthier you are, the more satisfied you are with yourself and your body. Conversely, the unfit person, male or female, is basically displeased with his appearance if not with his fitness. If you don't please yourself, it's hard to please others. Being "out of shape" and "unfit" has moral, physical and psychological connotations.

Two Camps

The whole world is divided into two camps; the doers and the non-doers. There are active non-doers like Ben Franklin who advised lying perfectly still in bed until all urge to exercise had passed, and there is a large group of passive non-doers who would really like to be doers but lack the required motivation and compulsive nature.

And then, there is a handful of people who have discovered animus—the life-giving spirit, and they are hooked. "My God, I'm alive, things are working like they should. My heart is beating, my lungs are delivering, my body is performing." It's fun to be alive, and it's real exhilaration, a true high.

Efficiencies

There are many ways of attaining this feeling, this joy of living, this animation. Running has the advantage of efficiency—most exercise per unit of time. Once conditioning has been completed you can maintain that level with fifteen minutes, three times per week. Even counting getting through the warmups, the cooling off, the shower and the drive home, it's still got to be less than two hours invested. Some further time efficiencies are possible if you run around the block at home instead of driving down to the "Y" or over to some school track. You get to know your neighborhood (and all the dogs thereof) much better. The neighbors wave as they see you approaching and draw circles with their hand after you have passed.

Dangers of Driving Home

It's actually very dangerous to drive home immediately after running. During a distance run nearly 50% of your blood volume is below your waist. Your "second wind" comes as pulmonary edema is relieved and the blood volume is shifted downward. If you are sitting on the grass after a run and faint from the abnormal distribution, then redistribution will occur as you are lying there. If you slip behind the wheel of a car before this volume displacement is readjusted, you can be in real trouble. With a loss of consciousness, the steering wheel keeps you flexed and the problem cannot correct itself.

University of Minnesota Study

People who run do so not because they enjoy it, but rather because somehow they are motivated to it; women usually for its cosmetic effects, men for its physical effects. The University of Minnesota did a beautiful study on this subject in 1969.[1] They took 400 average, fat, TV watching, cigarette smoking, middle-aged coronary prone male slobs and split them into two groups. The first group they let go their own dissolute way. The other group they motivated into a thrice weekly exercise program at the U—calisthenics, jogging, the whole bit.

At the end of two years, they had one more coronary among the joggers than among the sedentary group; but the rest of them wouldn't stop exercising. They all claimed that they felt better, slept better, looked better, were more vigorous, their wives loved them more, slower resting pulse, etc. All the study proved was that you could motivate people to exercise; and if the theoretical benefits didn't materialize, the individual would invent other reasons and con-

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*Minneapolis, Minnesota.
See editorial, page 105.

tinue exercising.

A jogging pathologist[2] maintains that running a marathon distance of 26 miles in four hours will protect you from a coronary for six years and that running 10 kilometers at an eight minute pace will protect you for two years. Non-jogging physicians tend to ignore these facts.

Confessions of a Jogger

So I'm a jogger, and in general am motivated toward an exercise program; but "in general" motivation won't get you started each time. The post-exercise exhilaration doesn't help either for that doesn't come till later, and you tend to forget about it when you are trying to think of reasons for not running today, or at least not "right now."

"It's too hot or too cold. Too windy, too wet, too dry, too dark, too icy, too early or too late. I'm just getting a cold; or I'm just getting over a cold; or I haven't eaten yet; or I just finished eating." Actually that last one is an absolute contraindication to running, for it completely ruins your time if you have to stop and throw up half way around the course.

I don't completely understand it, but one of the things that will ensure my running is if my wife mentions *any* of the above as reasons why I should not run. My virility or something is threatened, and off I go . . . "through rain, or snow, or sleet, or hail or dark of night". Another thing that helps to get started is having a buddy to run with. Days when his reasons not to run have overcome his compulsions, a call from you will get him out again and vice versa. Even a dog helps; but if you can keep from looking them in the eye, it's quite easy to forget that neither they nor you have had your exercise for the day.

Jogging Ploys

I have even heard tell of a mean-spirited jogger (not a doctor) who on occasion would plan his jogging so they would be late for a party he didn't want to go to in the first place. His wife was at least "one down" by this ploy for she couldn't really verbalize her anger with this behavior. After all, it was good for him and besides he was doing it for her too; he was running for his wife so she would be insured of his pleasant company in her old age. He also could get extra strokes when they got to the party late. Everyone would have to be told that his jogging was the reason they were late and—instant hero—the center of the conversation. Thus double, triple and even quadruple benefits would ensue from proper timing of the jog. No wonder this pernicious practice may soon spread even into the ranks of the medical profession.

Timing Your Jogging

Some people run in the morning, first thing. You really feel great the rest of the day, mostly because you don't have that damn run staring you in the face. I'm a diabetic, on the needle, and have a constant late morning hyperglycemia that is best cured by a mid-morning run. Too close to meals and I vomit, too far from meals and a "zukerkranken fit" ensues. Makes the planning somewhat more complicated, and a mid-morning run is not compatible with a busy office practice. I have thus settled on a day-off, Saturday and Sunday schedule which has the advantage of removing the decision about "Today, or can I put it off until tomorrow?", from the arena of self-contention, so that the only hassle is "Now, or can I put it off till later?"

Tricks to Prevent Jogging

When you eventually run out of excuses and delaying tactics and start off running, the battle has just begun. You will have to maintain your motivation and keep running. Your mind will play all sorts of tricks on you to get you to stop. Psychological tricks. "This is stupid. Imagine a 40-year-old man running around the block in the rain. Do you actually plan to keep this up three times a week? For the next forty years? Better stop and tighten your shoelace. Why don't you quit after a mile? Lots of people can't even run a mile. Why don't you walk for awhile; there's no sense in killing yourself when you are supposed to be doing something for your own good."

Tricks to Keep Running

To counteract these tricks the well motivated runner will develop a separate bag of tricks to keep him going, or to make him go better. Although, there is a natural inclination to hide yourself from public view when engaging in any sort of minority type activity, this is a mistake for a runner. Having people notice you is one of the fringe benefits. It is probably no coincidence that my favorite course goes right by the houses of three doctor-friends. They will commonly mention my athletic feats in the staff room, thus augmenting the fringe. I'm sure that I can run a little faster as I pass by their houses. You can also pick up your feet a little higher each time a car passes. It might be someone who knows you; and even if not, you have to uphold the honor of the jogging fraternity. (Non-joggers are wont to sneer when they see a jogger walking.)

While I am running, I try to think of things to keep my mind off how much I hate running. I started by counting steps, but was so anoxic that I couldn't remember what number I was on. As I became more conditioned, however, I started solving world problems whilst running. I can never remember the solutions (or even the questions) when I get home, but it takes my mind off the running.

Composing While Running

Sometimes I plan essays or talks for keepsake notebook entries in my mind. Beautiful, literary, articulate, precise works, full of polished concise phraseology; but as there is no way to write things down while running, I tend to forget them during that final dash up the driveway. It's like a dream, where if you could remember in the morning what you went through during the night, the Great American Novel would almost write itself. The trouble is—I just can't remember.

Variety Has Its Place

Variety helps keep things going, for besides its other disagreeable features, distance running is very boring. Running in different areas adds to the interest. When I take the kids to the arena for hockey, I run out there. In the summer at the pool, I drop the kids off and run before a swim. Sometimes I run on the golf course; sometimes a longer, slower course around the lake. When we go camping. I find a two-mile circle and run there. The only time that didn't work out so well was in the mountains. There was just no way I could go even a slow two miles at 9,000 feet.

Sometimes I pretend that I've got gears that can be easily shifted to make me go faster, or take longer steps with less effort. And you really fly the first run in the springtime when you do it without overshoes. Sometimes a stop watch helps; sometimes running without the clock and pretending that you are doing it just for fun is better. Taking off the hat at the half-way mark and the mittens one at a time during the last half mile gives cooling relief that can be as good as a third and fourth wind.

When you get the rhythm going on certain days, it seems like you could keep on going forever; barely breathing hard, just sailing along enjoying the feeling of being alive. Usually, though ,when I have that feeling, it means that I have been loafing and my time is nowhere near seven minutes. It's probably better exercise anyway to vary your speed from faster to slower rather than a constant middle pace; and that kind of variation helps break the monotony of the run into smaller, easily manageable segments.

It's much easier to run a familiar course so you can pace yourself and have a little left at the end for the final sprint. The first time over a course is much harder. There is a story of one marathon runner who broke into tears and was completely unable to finish when he learned that the finish line was really two miles further away than he had first been told.

Psychology of Running

The psychology of running is fun. A marathon race was won once when one of the leaders turned to the other and said, "I've never run a marathon before, shouldn't we be going faster?" The self-discipline of running is exhilarating. You get out there in spite of all the reasons for not running. You don't really like it; you're not feeling great and it hurts, but you do it anyway. You do what you made up your mind to do. You have to run that damn two miles. You have driven yourself, pushed yourself, disciplined yourself. When you are done you don't have anything you can sell, but you do have a most magnificent sense of self-satisfaction. Running of this type not only builds up physical stamina but has a great psychic component. Most of the great marathoners are ten years older than the dash men as it takes some extra maturity to endure the mental stress. Someone once said that a marathon isn't a race; it's an experience. Running that mile or two around the block has the same kind of rewards on a smaller scale. Rewards that are available to all of us.

Mental Discipline

Probably the mental discipline is as beneficial as the physical discipline; bringing your tired complaining body under the complete control of your mind and will. Making yourself go faster when you really want to go slower. It's a mystical, almost religious feeling. Probably akin to the feeling that produced hermits in other less crowded times. You just know that you are superior to the great mass of people who don't feel as you do. Anything that hurts so much and makes you feel so bad has got to be good for you. When it's finally over for the day, you are so healthy and virtuous that you can be lazy and overeat and still have a credit balance.

Dashing Conclusion

I apologize for the title being a bit of a come on, but only a few exercise nuts would have read an essay on the psychology of jogging. To sum it all up, the hope of virtue and the expectation of longevity are imaginary; the animus and the feeling of vitality are real; the discipline is beneficial; the exhilaration and the "super-high" that comes after the exercise are drug induced by your own adrenal cortex; and it's a great feeling. I recommend it.

References

1. Exercise in controlled trails of the prevention of coronary heart disease. From the Laboratory of Physiological Hygiene, University of Minnesota, Minneapolis, Minnesota.
2. Dr. Thomas Bassler, Editor of The Journal of the American Medical Joggers Association and Medical Examiner for Los Angeles County.

Dr. Haddow Keith Honored

Dr. Haddow Keith, received an award of appreciation recently from the Olmsted Association for Retarded Children. Dr. Keith, Mayo Clinic emeritus consultant in pediatrics, helped organize the Day Activity Center for retarded children.

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*Shakespeare, "Pericles," I.ii.67-69. c. 1608.

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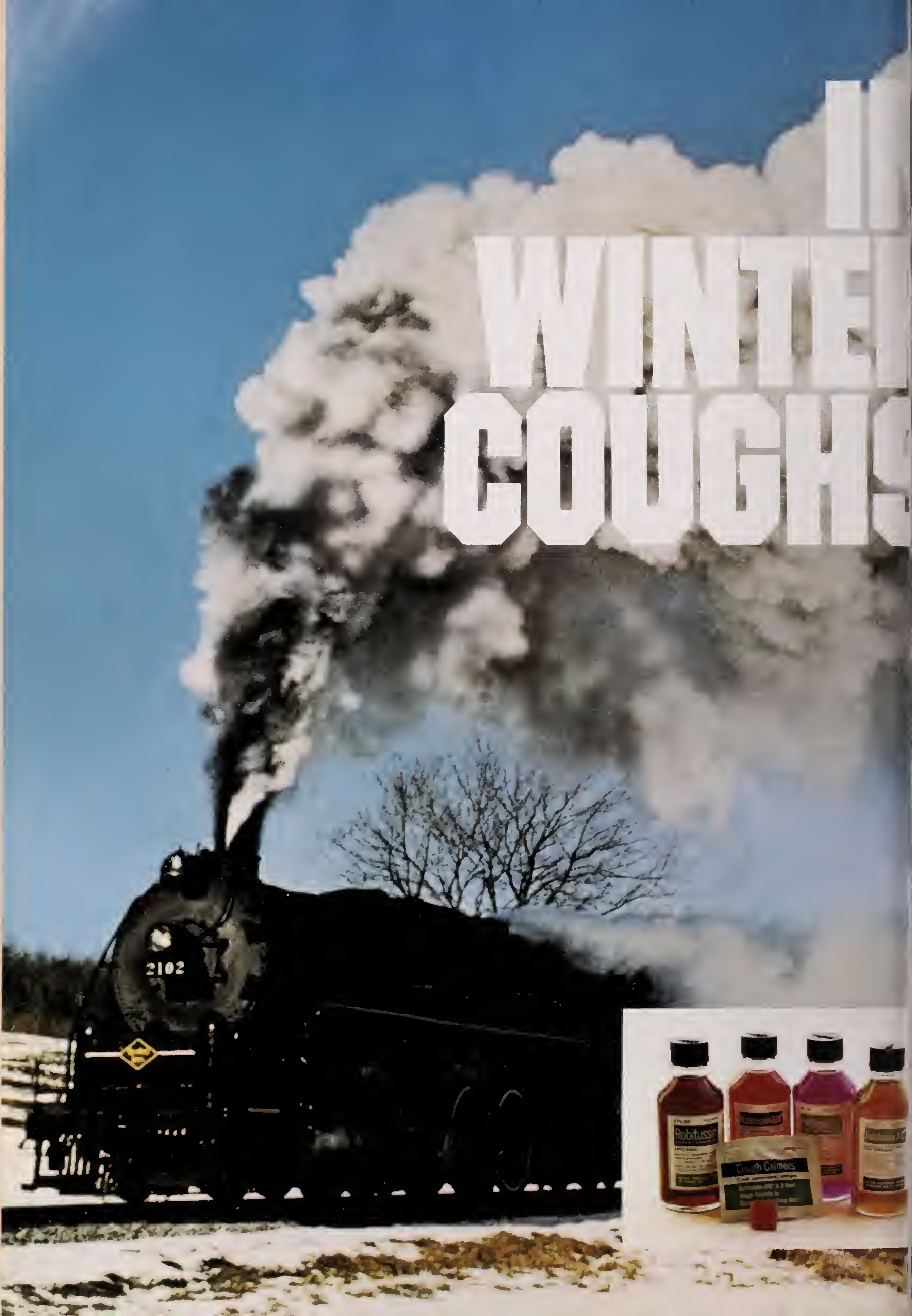
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l and pharmacy practice are thus
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elves guaranteed absolute protec-
on from unsafe drugs, or freed
hysicians, dentists and pharmacists
om their responsibilities to patients.
s a practical matter, however, such
ws and regulations encourage inter-
rofessional communications regard-
g drug product selection and assure
ach profession the opportunity to
xercise fully its expertise in drug
sage, to the advantage of patients.

Physicians and dentists should
e urged to increase the frequency
nd regularity of their contacts with
harmacists in selection of quality
rug products, recognizing that economies to patients can be improved through such communication, taking into account the patients' needs. The pharmacist's knowledge of the chemical characteristics of drugs, their mode of action, toxic properties and other characteristics that assist in making drug selection decisions should be utilized to the fullest extent practicable by physicians and dentists in serving their patients.

Since drug product selection entails knowledge derived from clinical experience, the physician's and dentist's roles in product selection remain primary and do not permit delegation of decisions requiring medical and dental judgments. A broader role in therapy will evolve for pharmacists as improved understanding and cooperation among the professions continue to grow.

There has been no evidence that there are convincing reasons to modify or repeal existing laws and regulations prohibiting the unauthorized substitution of another drug product for the one specified by a prescriber. It is our belief that such laws and regulations merit the joint support of the medical, dental and pharmaceutical professions and the pharmaceutical industry.

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Pregnancy Fantasies

HOWARD W. FISHER, M.D.* and IRVING C. BERNSTEIN, M.D.†

An exploratory study of the feelings of nineteen women about pregnancy was carried out. Third trimester primigravidas, married and unmarried, were compared to a split control group of women never pregnant and women not pregnant during the study.

Tentative conclusions reached are that some of these women were ambivalent about their pregnancy and that some used it to solve personality problems. Marriage provided a male figure that gave the woman reassurance and potential satisfaction during pregnancy.

Feelings about pregnancy are important in some psychophysiological illnesses.

STUDIES OF THE feelings of pregnant women are rare. Indeed, most physicians doing obstetrics avoid dealing with pregnant women's feelings. Further, there is little written in medical textbooks about pregnancy fears and fantasies.

It will be the purpose of this paper to explore the feelings of third trimester primigravidas, married and unmarried, comparing them to a split control group of women never pregnant (married and single) and women not pregnant at the time of this study (married and divorced, all with one child).

The literature is usually without controls. Freud[1-4] wrote of uncanny symbolization involving pregnancy. Deutch[5] wrote of "primitive fears" during pregnancy, adding that "conversions conceal pregnancy fantasies and express . . . (fears)." She noted that pregnancy is "unreal" since the abdomen is a "curtain." She implicated pregnancy fantasies in vomiting, anorexia nervosa, and motivation for surgery. She pointed out that a wish for pregnancy may not be the same as a wish for a child, and that a man can be used as an "accomplice" in a woman's fight with her mother. Fried[6] wrote a fascinating account of pseudocyesis, "the oldest known psychosomatic condition," in which he said there were no unconscious pregnancy fantasies. He noted that "false" pregnancy was used to solve a bad marriage. Klein[7] in a monograph of a pilot study on anxiety during pregnancy stated, "anxiety does not mean the pregnancy is unwanted." A group of women in his study were ambivalent about being pregnant but later accepted it. He felt "marital discord is important in the rejection of a pregnancy." Bernstein[8] in a paper on marriage therapy pointed out that during pregnancy the husband loses the "mother" he married, resulting in marital stress. He also found that many women reject their pregnancy at some point.[9] Menninger[10] noted the differences between conscious and unconscious fears. Kolb[11] states that psychosis is rare post-partum and especially rare in primiparas.

Methods

Four groups of women, a total of nineteen, were studied. Five unmarried primigravidas at Booth Salvation Army Hospital, five married primigravidas from the University of Minnesota Obstetrical Clinic, four women previously pregnant (three married, one divorced) from the Clinic, and five women never pregnant (two married, three single). The last group consisted of a patient from the Clinic, three secretaries from the Clinic, and one secretary from an outside pediatric clinic.

All subjects were white, ages 20-25, with at least a high school diploma. Several had college experience. All but one were third trimester primigravidas. One girl had had a spontaneous miscarriage in early pregnancy prior to her current pregnancy. All of the unmarried subjects

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Reprint requests to Dr. Fisher, 19 South First Street, B1806, Minneapolis, Minnesota 55401.

Read before the Minnesota Obstetrical and Gynecological Society, Duluth, Minnesota, May 5, 1973.

were giving up their babies for adoption.

The subjects were told only that they were participating in a study about pregnancy done by a psychiatrist. Clinic charts were screened for pertinent control data. Selection was otherwise random.

Techniques

Three techniques were used. A 30-minute personal interview, a questionnaire, and non-standardized projective testing.

An initial interview followed a brief explanation of the study and reassurance of confidentiality. All subjects showed little resistance and marked enthusiasm about being allowed to express their feelings. The questionnaire was designed to explore areas possibly not covered in the interview. Ten pictures serving as a non-standardized projective series were administered. One Booth girl and one married woman in each control group did not complete this.

Results

This study would support that feelings during pregnancy are important. The first finding was that all the women feared pregnancy and were in some degree of conflict about it consciously or unconsciously. The most important difference was whether the fear was predominantly conscious or unconscious. The intensity of the fear was also significant.

The most threatening fear was the fear of loss or of separation from the child. If the fear was unconscious and intense, it seemed to be avoided by various means to protect the personality from pain or damage during the "process" of pregnancy and childbirth (separation). These defenses included infertility, adoption, or strong wishes for anesthesia or hypnosis during delivery. One subject found the loss so intolerable that she developed post partum urinary retention as a symbolic equivalent of continued pregnancy. The same subject had been infertile previously. Fear of psychosis incident to the loss was common in all groups.

The Booth women were all depressed about the loss of their babies, since they were forced to give them up for adoption.

Fear of a malformed or damaged infant was also common. The dynamics were clearest in a Booth girl who associated the fear to feelings that her pregnancy was incestual.

Another major fear was that the infant would make the husband so jealous that divorce would ensue following delivery.

"Use" of Pregnancy

The other major conclusion from the data was that these women used pregnancy to solve personality problems. Adaptive use occurred only within marriage. *Non-adaptive "Use":* There seemed to be a fundamental drive toward pregnancy in every subject but the motivation for pregnancy seemed to differ. Non-adaptive use of pregnancy included a number of means that were fundamentally hostile. Some of these women sought marriage to avoid a "total loss" or with rationalization that it was "for the sake of the child." These women had low self-esteem and seemed to use pregnancy to fill a sense of emptiness. Pregnancy was an attempt to establish something inside the self. Once felt, they wished the "fullness" to continue. Several women acted as though their actual children had no reality to them. These women seemed to need a continuous symbiotic relationship, totally exclusive. Once achieved, they withdrew from their husbands, claiming frigidity.

The Booth mothers demonstrated the search for the solution to the oedipal curiosity of what it feels like to be pregnant. They seemed to use pregnancy "to make someone care," to have a doll, playmate, possession, or sibling and out of envy of a girlfriend's pregnancy; also, because of feelings that the self was worthless and in need of "rebirth," or to escape from the self, felt to be in trouble. Non-adaptive pregnancy was by definition a solution that did not lastingly elevate self-esteem.

The Booth mothers did not marry the biological "father," in contrast to several of the married women who had out-of-wedlock pregnancies but married the man involved (allegedly). Those women who married seemed less angry at men, generally. Also, there seemed to be a difference in that there was a man around who consented to "father" the baby within a family structure.

The Booth girls demonstrated that "the baby comes first, the marriage second," i.e., that pregnancy was used to gain security. Also, there seemed to be an expectation that they would have to give up the baby in advance—"It doesn't belong to me."

Of the married primigravidas, only one woman aid her pregnancy was "planned" (presumably neaning that her husband had been consulted). Three of these women had "unplanned" pregnancies; two had been pregnant out-of-wedlock but "allegedly" married the biological father.

Adaptive "Use": The only adaptive use of pregnancy seemed to be within a stable marriage, allowing the woman to make a "gift" of the baby o her husband, simultaneously satisfying her ense of femininity and her husband's sense of nasculinity. Once accomplished, strong reassurance to the self occurred, producing a profound ense of security in the woman. Movement of he child in utero was viewed as affirmation of "normality," proof of femininity and masculinity. These feelings may explain why some women have many children. They like the feeling of beng pregnant, although not necessarily the presence of actual children.

This study was meant to be exploratory. Only nineteen subjects were involved. Complex and fascinating fantasies were present in each subject. Many derived some therapeutic benefit from simply expressing their feelings about being pregnant.

Discussion

This study would support initial conclusions that many women fear pregnancy, consciously or unconsciously, and some use it as a solution for personality problems. They need it as well as fear it. It would seem to be the time of greatest pleasure and the time of greatest fear. When the conflict is strong and unconscious, physiological symptoms can be precipitated, including infertility and post partum urinary retention. When the fear is more intense, psychosis incident to the loss was seen to be avoided through the protection of infertility. Physicians who have patients threatened by these fears may need the assistance of a psychiatrist in understanding and accepting them.

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Pediatric Day

Pediatric Day will be held March 16 at the Mayo Clinic. The program will be comprised of a series of talks by the Department of Pediatrics of the Mayo Clinic and Mayo Medical School relating to problems in pediatric practice.

Dr. John D. Nelson, Professor of Pediatrics at the University of Texas, will be the guest speaker and will speak on subjects relating to pediatrics and infectious disease.

Write: Dr. E. C. Burke, Professor of Pediatrics, Program Director, Mayo Clinic, Rochester, Minnesota, 55901 for information.

"Seven years and six months!" Humpty Dumpty repeated thoughtfully. "An uncomfortable sort of age. Now if you'd asked *my* advice, I'd have said 'Leave off at seven'—but it's too late now."

"I never ask advice about growing," Alice said indignantly.

"Too proud?" the other enquired.*

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*Lewis Carroll: Through the Looking-Glass. "Humpty Dumpty." 1887.

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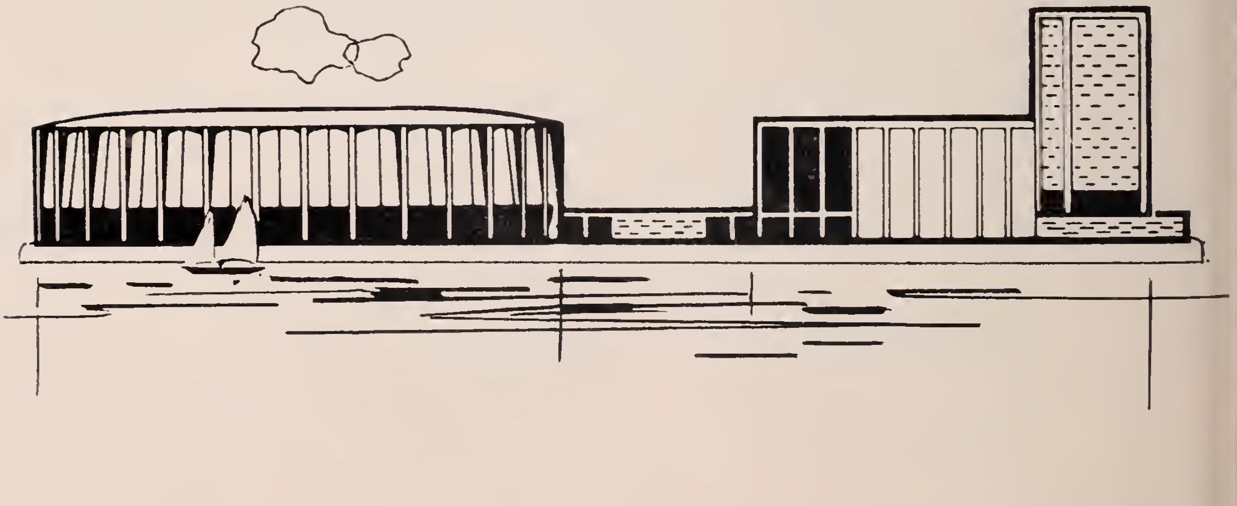

Review

Stasis Ulcer

Diagnosis and Treatment

KARL A. LOFGREN, M.D.*

Stasis ulcer is a common, often disabling, complication of chronic venous insufficiency (or postphlebitic leg). The pathophysiology, differential diagnosis, nonsurgical and surgical management are discussed from the author's own experience with this problem at the Mayo Clinic.

STASIS ULCER is a common, often disabling complication of chronic venous insufficiency reputedly afflicting 500,000 people in the United States alone. The lesion usually develops in the postphlebitic leg many years after the initial episode of deep thrombophlebitis. Stasis ulcer may be defined as an open defect of the skin and subcutaneous tissues brought on by venous stasis. Synonyms include gravitational, indolent, postphlebitic, varicose, and venous ulcer, but the term "stasis ulcer" seems more appropriate because it is descriptive of the basic underlying venous pathophysiology.

Diagnosis

A prerequisite for the correct diagnosis and proper treatment of stasis ulcer is an understanding of the pathophysiology of the venous system in the lower extremity. When veins become incompetent from the destructive effects by thrombophlebitis on their valves and elastic walls, normal venous return is impeded and venous hypertension and disturbance of capillary exchange result with harmful sequelae in the postphlebitic limb. Although the resting venous pressure in the leg in the upright position remains normal, the ambulatory venous pressure is grossly elevated. Effects from pathologic stasis gradually develop in the skin and subcutaneous tissues in the presence of chronic venous hypertension. Pigmentation, dermatitis, induration, cellulitis, and ulceration are progressive stages of stasis that often develop over many years in the postphlebitic condition. These manifestations occur more often over the medial aspect of the lower leg and ankle where the larger perforating veins also may be present. When the perforating vein is incompetent, the elevated pressure in the incompetent deep veins is transmitted directly into the superficial veins, compounding the congested condition already present in the skin and subcutaneous tissues. A trivial injury to the skin of the lower leg or ankle often will precipitate a slow-healing lesion which becomes a chronic ulcer unless treated adequately.

The diagnosis of stasis ulcer is based on the history and on the presenting findings. Often the history leads back to an episode of iliofemoral thrombophlebitis or "milk leg" that had complicated pregnancy, operation, or major fracture. The history may be negative for phlebitis, but the signs of dependent edema, stasis cyanosis, and distended superficial veins still support the *clinical* diagnosis of chronic deep venous insufficiency. In a survey of 129 patients who had large stasis ulcers treated surgically at the Mayo Clinic, only 70 (54%) had a positive history of deep thrombophlebitis while 110 (85%) showed clinical evidence of chronic deep venous insufficiency (postphlebitic leg).[1]

The location of stasis ulcer is typically in the "ulcer-bearing area" around the ankle and lower third of the leg, more often on the medial than on the lateral aspect. If the lesion occurs above this area, other ulcerations of different etiology must be considered in the differential diagnosis.

Typically, the ulcer is surrounded by a wide zone of induration, pigmentation, and inflammatory edema. The base of the ulcer usually is covered with a grayish exudate, but underneath are granulations that bleed easily. Nonpathogenic bacteria from surrounding skin flora abound in a harmless manner. The depth of the ulcer will vary, but it never will extend down through the underlying layer of deep fascia. Its size may range from a tiny, encrusted lesion to a huge ulceration that encircles the lower part of the leg. It is not unusual for several stasis ulcers to occur on one or both legs.

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*Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Read at the meeting of the Minnesota Surgical Society, Duluth, July 20, 1973.

The differential diagnosis includes lesions that resemble stasis ulcer by location or appearance but may instead be caused by trauma, ischemia, infection, blood dyscrasia, malignancy, or other rare disorders. Ulcers caused by trauma alone usually occur on the anterior aspect of the leg where superficial injuries are most likely to be inflicted. They heal more rapidly in the absence of venous stasis. Ischemic ulcers are typically painful on elevation of the leg, and their response to treatment is extremely slow. They also often occur below the malleoli and on the feet. Absence of inflammatory induration and lack of granulations in the base of the ulcer are typical findings, often with diminished or absent peripheral pulses of the foot and blanching of the skin on elevation.

Among the ulcers caused by ischemia are also the rare hypertensive lesions, small but painful defects with an underlying pathologic condition of occlusive disease of arteriolar rather than arterial vessels. These infrequent lesions occur higher on the leg than stasis ulcers. Ulcers caused by infections such as syphilis and blastomycosis or by blood dyscrasia (sickle cell anemia, polycythemia, and others) are not common, and serologic tests and blood-smear examinations are necessary for the establishment of diagnosis. Pyoderma gangrenosa is an infrequent ulceration, extensive and necrotic, often associated with ulcerative colitis. Biopsy of nodular ulcerative lesions is necessary to rule out malignancy.

Treatment

Treatment is aimed at relieving the underlying stasis and at healing the ulcer. This includes nonsurgical as well as surgical measures. In ambulatory patients, elastic compression is often adequate treatment for minor uncomplicated ulcers. The Elastoplast boot has proved effective for the small, shallow ulcer less than 2.5 cm in diameter. Gauze, cotton padding, and Elastoplast bandaging are applied and should be reinforced by an ordinary elastic bandage from toes to knee when the patient is ambulating. The Elastoplast boot is removed and replaced as needed every seven to 10 days until the ulcer has healed. After the ulcer is healed, the patient must continue to use elastic support to prevent recurrence and to control the underlying venous insufficiency. Smaller stasis ulcers will heal readily with rest in bed, elevation of the extremity, and local application of moist dressings (0.25% aqueous aluminum subacetate solution). Many of these patients may also have incompetent perforating and superficial veins that are best treated by surgical removal in order to lessen the local venous stasis.

Skin grafting generally is indicated for larger ulcers in order to shorten the healing time and the hospitalization. Preoperative treatment of the stasis ulcer includes rest in bed, elevation, and moist dressings until the ulcer bed appears clean with pink granulations and the serous drainage has subsided. During operation, the granulations are shaved down to the deep fascial level and the raised, fibrotic edges of the ulcer are beveled with the scalpel, leaving a smooth ulcer bed for the graft. The deep fascia is *not* excised. It provides needed support to the musculovenous pump mechanism of the leg, and by leaving it intact a better functional and cosmetic result is obtained. The skin graft is taken from the anterolateral surface of the thigh with the dermatome (the Brown electrodermatome).

The ulcer bed must be absolutely *dry* for a successful graft, and all oozing must be stopped with gentle pressure and elevation. If necessary, a thrombin solution can be used to control capillary oozing (5,000 NIH units of thrombin in 5 ml of physiologic saline solution). The split-thickness graft, preferably in one piece, is laid down over the ulcer, slightly overlapping the edges of the lesion. Sutures are not used for they traumatize and may cause oozing. The graft is held in place with a layer of moist, fine-mesh gauze; sterile bandages (Kerlex); cotton pads; and a four-inch elastic bandage. Rest in bed with the legs elevated about 15° follows for 10 or more days, after which the graft has normally taken so the patient can leave the hospital.

Vein surgery is indicated when incompetent perforating and superficial veins occur in conjunction with the stasis ulcer. Rarely, however, are varicose veins alone responsible for the ulcer. Vein surgery and skin grafting can be done as a combined procedure or vein surgery alone may be sufficient if the ulcer is small or nearly healed. When significantly incompetent superficial veins are eliminated, much of the local congestion in the ulcerated area is often relieved. At the Mayo Clinic the practice is to ligate and resect the incompetent perforating veins where they emerge through the underlying deep fascial layer. The suprafascial approach is preferred because it makes it possible to remove the adjoining varicosities in the subcutaneous layer. The greater or lesser saphenous vein also is usually removed whenever the preoperative examination shows it to be incompetent.

Elastic support is ordinarily necessary to prevent recurrence of stasis ulcer. It provides the needed additional support to the musculovenous pump mechanism and the insufficient deep venous system. Adequate elastic support will prevent and relieve stasis of the lower leg and ankle in the "ulcer-bearing area." Combined with periodic follow-up examinations, it serves a vital function in the successful long-term management of the healed ulcer.

Summary

Understanding the pathogenesis of stasis ulcer aids immensely in the diagnosis and treatment. Skin grafting of larger ulcers and surgical removal of incompetent perforators and superficial varicosities are effective surgical measures of treatment. Adequate elastic support to the leg is usually required for the underlying chronic venous insufficiency in order to prevent recurrence of the ulcer.

Reference

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Community Referral Sources

A number of sources are available to physicians seeking information on community service organizations for referral purposes. The following is one such source:

Hennepin County Alcoholism, Inebriety, Drugs
Information and Referral Services
527 Park Avenue, Minneapolis
Phone: 348-8013

Services	Days/Hours	Eligibility	Fees
Telephone answering service	24 hours/day 7 days/week	Hennepin County resident	None
Counseling (appt. preferred)	8 am—4:30 pm Mon, Wed, Thurs, Fri		
Diagnosis, information, referral for the chemically dependent person, their family, other concerned individuals & community agencies	Appointments for each service are arranged		
Family planning for intervention in a chemical dependency program			
Counselor Training for educational institutions			
Informational seminars for community & professional groups			
Family & concerned persons group			
Follow-up for Hennepin County residents discharged from Anoka State Hospital Chemical Dependency Program			

This is a program of the Hennepin County Alcohol & Inebriety Program Office

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Community service directories are available from the Community Health and Welfare Planning Councils in Minneapolis and St. Paul. For a directory of metropolitan youth-serving agencies, The Catalogue can be obtained from Enablers, Inc., 1238 Baker Building, 706 Second Avenue So., Minneapolis, Minnesota 55402.

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A Look at the Family Planning Nurse Practitioner

EVELYN E. HARTMAN, M.D.*

The training program herein described, was planned and carried through for the specific purpose of providing skilled nurse practitioners to overcome the shortage of medical manpower in the Minneapolis Health Department's family planning clinics. The quality of the services being rendered by the family planning nurse practitioners has amply justified the project. Didactic teaching was provided, in combination with an individualized, supervised experience.

CHANGES ARE occurring in the traditional roles of physicians as well as nurses. By expanding their own roles nurses are taking over some of the responsibilities commonly held to be those of the physician. As with anything new there is some confusion and controversy over this change. The physician may consider such a nurse as his assistant, but among most nursing circles it is felt that the nurse continues to function as a nurse but with expanded responsibilities. This is the concept that is held in relation to the family planning nurse practitioner program in the Minneapolis Health Department.

Family planning services have long been available, but only in recent years have they become a regular part of health department services. They have become *the* part that is most rapidly expanding. The need for medical manpower to provide these services is increasing proportionately. Health departments must compete with other agencies, such as Planned Parenthood and public and private hospitals to obtain the services of physicians to serve the increasing numbers of women requesting family planning services. There are few physicians who relish the monotonous chore of working in a public family planning clinic with its lack of challenge and interesting cases. It is almost impossible to obtain certified nurse midwives for these clinics, because they are largely unavailable in the midwest part of the country. Yet such clinics are needed to serve the many low income women who cannot afford and are not eligible for private care through the auspices of county welfare departments.

In order to meet the shortage of medical manpower and at the same time to continue to provide quality health services, the Minneapolis Health Department and Hennepin County General Hospital cooperated in development of selection criteria and in training candidates as family planning nurse practitioners for Minneapolis Health Department clinics, as well as developing standing medical orders under which these nurses would function. Ideally, this training should have been provided by the medical and nursing departments of a university. However, since this was not yet the case, and since without additional manpower, the already established health department family planning services would need to be curtailed, the training program herein to be described was instituted as a stop-gap procedure.

The four nurses that were selected for the training were chosen from among those that had volunteered. They had all graduated from at least a diploma course, had many years of hospital and clinic nursing experience and had previously worked in the Minneapolis Health Department family planning clinic in the traditional role of a nurse. In addition they were emotionally mature women and had enjoyed their job.

The training program for the nurse candidates consisted of three components:

First, the nurses participated in a course conducted by General Hospital for their own nurses as well as for nurses from other agencies in the community. The course consisted of a series of twenty hours of medical lectures by an obstetrician covering topics such as anatomy and physiology of the reproductive system, pelvic and breast examinations, family planning and gynecological histories, physiology of the menstrual cycle, con-

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*Former Director Maternal & Child Health Minneapolis Health Department, Minneapolis, Minnesota.
Presently practicing in Prescott, Arizona.

ception, principles of contraception and methods, contra-indications to contraception and infections. Concurrently another twenty hours were spent in applying this knowledge in practice in the family planning clinic setting at the hospital.

Secondly, the nurses participated in a ten-week series of two hour discussions conducted by a maternity nurse specialist in the Minneapolis Health Department covering the following topics: birth control methods, adolescence, morality, masculinity and femininity, contraception: acceptance or rejection, human sexuality, sexual misuse of the partner, and interconceptual care. This last topic was included because the Health Department considers family planning a part of interconceptual care in the complete cycle of good maternal and child health. The classes also covered the feelings of the nurses toward family planning, awareness of the patient's non-verbal communication and her body language, consideration of the factors in the patient's environment that might have an influence on the patient's motivation for contraception. These topics were considered important because of the hang-ups of the nurses themselves. The nurses were all from middle class, conventional backgrounds and felt uncomfortable, for example, when single girls of the age of their own daughters requested services or were diagnosed as having venereal disease. They also needed help in evaluating the many factors in the patient's life-style and circumstances, so different from their own, that might have an effect on the patient's ability to carry out instructions. Interviewing techniques were also discussed.

Thirdly and finally, the training program provided clinical experience in the Health Department's family planning clinics under the direct supervision of the clinic obstetricians and the Health Department's part-time certified nurse midwife. Each nurse progressed in the clinical experience at her own pace until she felt comfortable in her role. The nurses needed much time and experience with a substantial number of cases before they felt adequate, especially in doing a satisfactory bimanual pelvic examination and in being able to differentiate between what was normal and what was abnormal.

At the end of the training each nurse was evaluated by an obstetrician and the maternity nurse specialist and had to pass an examination to determine her ability in meeting the objectives of the Health Department in family planning in accordance with safe medical and nursing practice. According to these objectives the family planning nurse practitioner must be able to identify normal and abnormal physical, social and psychological conditions and refer patients with abnormalities to the physician, social worker, and others as indicated. Continuing evaluation is made of the nurse practitioner to ensure that she provides quality care to the patient. This evaluation includes spot checks by the physician to see that no medical problems have been missed by the nurses; continuing nursing supervision; and record audits.

Having completed her training the family planning nurse practitioner thereafter functions as the primary care person for the family planning patients who have been assigned to her by the clinic physician. The physician performs the initial medical examination and determines that the patient has no abnormalities either in relation to the contraceptive method to be prescribed or in her general well-being. The patient is then, after the initial visit, scheduled to see the nurse practitioner once a year for an annual check-up and every six months or oftener to receive her birth control supplies and for an interim health history. At all times the family planning nurse practitioner is under medical direction for her medically related responsibilities and functions under standing medical orders. The physician continues to be responsible for any medical treatment that might be needed and for writing medical prescriptions.

In her role as the primary care person the family planning nurse practitioner tries to evaluate the patient in all aspects that might influence her ability to attain her family planning goal. In order to accomplish this, the nurse first reviews the patient's record for past significant findings. She follows this with an interview to obtain a medical history on possible venereal diseases, general medical conditions, and symptoms that might constitute a contraindication to continuing with birth control pills. The medical history elicits information on such things as varicose veins, thrombophlebitis, weight gain, menstruation, spotting and dysmenorrhea, dizziness, headaches, edema, nausea and vomiting. The nurse practitioner also queries the patient about her own feelings and those of her mate toward contraception and planning for further children. If the mate has an antagonistic attitude toward birth control a referral is made to the clinic social worker. This may be due to the man's unconscious feeling that birth control constitutes a threat to his manhood. The nurse must be prepared to deal with the patient's questions, even to explaining the difference between the effects of estrogen and progesterone, as has happened. She must be honest enough to admit when she cannot handle a question or a problem and is in need of consultation or needs to refer the patient to someone else.

Prior to the annual physical check-up the patient has laboratory tests which routinely include a hemoglobin or hematocrit, a urinalysis for albumin and sugar, and a serology for syphilis. Other tests may be ordered by the nurse as indicated. The hematocrit and urinalysis results are immediately available to the nurse.

The annual physical check-up done by the nurse includes examination of the breasts for possible tumors (with the nurse at the same time teaching the patient how to do self breast examination); palpation of the abdomen; and a bimanual pelvic examination which includes the external genitalia, vagina, cervix, fundus and adnexa. At this time the nurse also takes a GC culture and a Pap smear.

If the health history, laboratory tests and check-up indicate that there are no complications the patient is continued on the pills earlier prescribed by the physician. The nurse reinforces instructions again on the method and reviews any possible side-effects that might occur. The patient is also given the A.M.A. pamphlet on adverse reactions. For the patient who has had an I.U.D. previously inserted by the physician, the nurse checks that it is in place. She herself never inserts it.

If, on the other hand the patient has problems in relation to the birth control pills or the I.U.D., the nurse always discusses this with the physician and he may request that the patient be returned to him. Consultation is available to the nurse at all times by the physician, the social worker, the agency nutritionist and the nursing consultant. The nurse consults with the physician on all medical conditions, even those unrelated to birth control. A report of trichomonas might be received from the laboratory, in which case the physician writes a prescription for treatment. The nurse explains the treatment to the patient and suggests possible preventive measures against re-infection.

Referral to the agency nutritionist is indicated when the nurse finds poor family diets or for the obese patient who is usually on a high carbohydrate diet. The nurse makes a referral to the clinic social worker when she finds a family in difficult financial circumstances. The social worker in turn, is able to direct the family to other agencies in the community for help. These examples at first glance seem unrelated to family planning. They have been revealed in the nurse's evaluation of the patient's total situation. They should be considered a part of interconceptual care in order to get the patient into the best possible state of health before she plans for more children. This service goes beyond the purely physical check-up and would not ordinarily be done by the physician.

Patients are encouraged to call their family planning nurse practitioner between scheduled clinic visits if they have questions or problems. The nurse, on the other hand calls the patient when she receives a report of abnormal laboratory tests, including venereal disease and positive Pap smears and arranges for follow-up care.

If the patient has no telephone, as frequently happens, the contact is made by a visiting or public health nurse through a home visit. In case of venereal disease, even gonorrhea, the mate is referred to the venereal disease clinic for examination and possible treatment and the venereal disease control officer of the Health Department is notified.

The family planning nurse practitioners have been generally well accepted by the patients. This was due first to the preparation by the physician of the patient being assigned to the nurse practitioner. The physician explained the nurse's function and reassured the apprehensive patient that she would receive good care. The one patient in the first few months of the program in 1972 who refused to be assigned to the nurse practitioner was a nurse herself. The patients have expressed their satisfaction with the nurse practitioner. They feel they are getting good personal care since they need to relate only to the one primary care person, rather than to a succession of different persons as so often happens in a public clinic. They also feel that their questions and concerns are being sympathetically, as well as professionally answered and that they are not being rushed through the clinic.

The clinic physicians have also wholeheartedly accepted the nurse practitioners after some initial misgivings. They have enjoyed their initial role as teachers of the nurses. They feel more job satisfaction when they now have the time to spend with problem cases and are not bogged down with the monotony of having to see all the routine, normal patients.

Since the family planning nurse practitioners function under standing medical orders, and are required to refer all patients who exhibit abnormal conditions, and they provide no treatment, there has been no problem as regards their licensing.

Don Juan: Their art is simply making faces. All they do is take the credit for lucky success; and you can profit, like them, from the sick man's good fortune and attribute to your remedies everything that came about through the favors of chance and the forces of nature.

Sganarelle: What, sir, are you impious about medicine, too?

Don Juan: It's one of the great errors among humans.

Sganarelle: What! don't you believe in seneca and cassia and emetic wine?

Don Juan: What do you want me to believe about them?

Sganarelle: You have the soul of an infidel. Still, you see that for quite a while emetic wine has been making a noise. Its miracles have converted the most incredulous souls; it's not three weeks since I myself saw a marvelous effect.

Don Juan: Well?

Sganarelle: There was a man who'd been in agony for six days; no one knew what to tell him to do, and none of the remedies did anything; at last someone suggested they give him an emetic.

Don Juan: He recovered?

Sganarelle: No, he died.

Don Juan: An admirable effect.

Sganarelle: What! for six whole days he couldn't die, and that made him die in an instant. Do you know anything more efficient?*

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*Moliere: Don Juan, Act III Scene 1, 1665.

Alcoholism

Alcoholic Detoxification

A One-Year Experience

J. J. GARBER, M.D.;* E. V. DOLANDER, R.N.† and J. D. DEXTER‡

Evidence has been presented which suggests a detoxification center with limited, though interested, staff can provide an adequate initial approach to the chronic alcoholic.

EFFECTIVE JULY 1, 1971, public drunkenness was no longer a criminal offense in the State of Minnesota.[1] As a corollary, provisions were made for the establishment of receiving (detoxification) centers for the initial medical care and counseling of inebriates.[2] The Zumbro Valley Mental Health Center, Rochester, Minnesota, in conformity with these laws, established a ten bed detoxification center. This report is intended to review the first year's experience.

Acute detoxification has been described in a general hospital setting,[3-10] but has not been reported in a non-hospital affiliated facility. It was apparent at the outset, therefore, that two primary questions required evaluation: (1) Can such a center accurately diagnose chronic alcoholism and initiate proper therapy? (2) Can an essentially non-medical facility properly deal with the initial medical needs of the chronic alcoholic?

Materials and Methods

All admissions to Zumbro Valley Mental Health Center Detoxification Unit from July 1, 1971, to June 30, 1972, were evaluated. Patients were assessed as to age, sex, marital and occupational status, length of stay, source of referral to the unit, condition on admission, county of residence, medical disposition, and subsequent alcoholic therapy.

The Detoxification Unit is staffed by (a) alcoholism technicians who provide all primary evaluations and care (b) a registered nurse (c) "on call" physicians. The technicians are recovering alcoholics, some of whom were detoxified at the Unit. They received in-service training, and attended a 45 hour course (18 weekly two and a half hour sessions) provided by the University of Minnesota Extension School. In addition, the technicians attended a 72 hour course at the University of Minnesota on Chemical Dependency. The registered nurse provided four hours service per day, supervising the detoxification unit.

During the period from August 2, 1971, to November 15, all admissions were seen by a physician. The remainder of the admissions were seen by a doctor on request of a technician. These two groups of patients provided comparison groups to assess the effectiveness of physician versus technician screening of serious medical problems.

Results

During the study period from July 1, 1971, to June 30, 1972, there were 554 admissions. This represented 329 individual patients and 195 repeat admissions (33.2%). The latter included 80 patients.

Age, Sex, and Marital Status

There were 487 male and 67 female admissions. The age range was from 13 to 79 years.

Of the 554 admissions 221 were married, 141 single, 143 divorced, 30 separated, and 19 widowed. Therefore, 60.1% were unmarried.

Employment

One hundred eighty-three (33.0%) were employed, 57 (10.3%) retired, and 232 (41.9%) unemployed. There were 15 housewives and seven students.

Length of Stay and Referral Source

The average length of stay was 44 hours.

Referrals to the Unit included 325 from the local police and other law enforcement agencies. There were 229 "voluntary" (patient, friend, or

---

*Internist, Olmsted Medical Group; Consultant to Zumbro Valley Detoxification Unit.
†Director, Zumbro Valley Detoxification Unit.
‡Zumbro Valley Detoxification Unit.

relative) admissions. (Table 1)

TABLE 1
Referral Source

	Number	Percentage
Local Police	242	43.7
Other Law Officers	83	15.0
"Voluntary"	229	41.5

Geographic Distribution

Patients seen were primarily from Minnesota (97.5%) and of those 79.1% were from a two county area. Two and five-tenths percent were out of state residents (Table 2).

TABLE 2
Residence

	Number	Percentage
Olmsted County (Rochester)	381	68.5
Goodhue County	57	10.6
Dodge County	20	3.4
Rice County	18	3.1
Fillmore County	16	2.9
Hennepin County	14	2.5
Other Counties	34	6.1
Out of State	14	2.5

Condition on Admission

At the time of admission 453 (81.8%) were intoxicated with alcohol, 46 (8.3%) were intoxicated with alcohol and other drugs, 47 (8.5%) were in withdrawal from alcohol alone, 8 (1.4%) were in withdrawal from alcohol and other drugs.

Referral to Alcoholism Therapy

Of the total admissions, 121 (21.9%) were transferred to primary treatment centers (three weeks or longer of intensive therapy) and 9.9% entered into other verified planned programs for continued sobriety. These included, then 163 admissions (31.8%) of the totals. These did not include referrals to Alcoholics Anonymous which could not be adequately assessed.

Medical Evaluation

Two hundred thirty-nine (43%) of the admissions received a complete medical examination by a physician. Of these, 189 (34.3%) were consecutive examinations during the period from August 2, 1971, to November 15, 1971.

There were thirty admissions transferred to a hospital for evaluation and care for a variety of medical and surgical disorders. Fifteen of the 189 seen consecutively by a physician were referred and 15 of those seen initially by an Alcoholism Technician and then on request in consultation by a physician (Table 3) were referred to other medical or psychiatric facilities.

TABLE 3
Reasons for Referral to Other Medical or Psychiatric Facilities

	Technician Screened	Physician Screened
1. General Medical Evaluation	3	5
2. Facial Trauma	3	..
3. Orthopedic Disorders	2	..
4. Psychiatric Disorders		
Psychoses	..	2
Depression	2	1
Psychoneurosis	..	1
5. Obstructive Lung Disease	..	2
6. Hypoglycemia	..	2
7. Bilateral Subdural Hematoma	1	..
8. Seizure Disorder	1	..
9. Acute Myocardial Infarction	1	..
10. Hepatic Failure	..	1
11. Epigastric Pain	..	1
12. Oral Carcinoma	1	..
13. Tuberculosis (under therapy)	1	..
	15	15

Discussion

The change in legal status of public drunkenness in Minnesota and the legislative mandate to establish receiving centers allowed a minimum of time (two months) and money ($500,000.00 for the entire state) to organize twenty-five receiving centers. These limitations necessitated opening a facility with a minimum of trained counselors and medical staff. We were concerned whether a receiving center such as this could provide initial alcoholic diagnosis and counseling preliminary to a primary treatment center referral as well as satisfactory medical triage?

Nearly one-third (31.8%) of the patients entered into an alcoholism treatment program. In the one year period prior to opening the Unit 644 public drunkenness arrests were made in Olmsted County. None of these entered into treatment directly from the courts. The primary intent of the law was to provide routes into therapy for the chronic alcoholic who had been largely ignored by the courts in the past. This has been provided by the receiving center.

Adequate medical screening has been accomplished. Fifteen (7.9%) of 189 patients consecutively seen by a physician were referred to a hospital for further evaluation whereas 15 (4.1%) of 365 patients screened first by an alcoholism technician were referred. Though this represents an expected difference in referral rate, the difference is of borderlne statistical significance ($p = 0.05$). Two points are apparent: (1) There were no mortalities in the Unit. (2) Several serious conditions such as bilateral subdural hemaomas, myocardial infarction, and the oral carcinoma were recognized so that medical consultations were obtained and hospital referral accomplished. Several patients having multiple (though not emergent) medical problems were referred to their local physicians. Two deaths are known to have occurred in patients after leaving the Unit (one suicide and the oral carcinoma, of metastases). Each occurred after referral to a hospital.

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Last night I suffered horribly—from an indigestion, I believe. I *never* sup—that is, never at home. But, last night, I was prevailed upon by the Countess Gamba's persuasion, and the strenuous example of her brother, to swallow, at supper, a quantity of boiled cockles, and to dilute them, *not* reluctantly, with some Imola wine. When I came home, apprehensive of the consequences, I swallowed three or four glasses of spirits, which men (the venders) call brandy, rum, or hollands, but which gods would entitle spirits of wine, coloured or sugared. All was pretty well till I got to bed, when I became somewhat swollen, and considerably vertiginous. I got out, and mixing some soda-powders, drank them off. This brought on temporary relief. I returned to bed, but grew sick and sorry once and again. Took more soda-water. At last I fell into a dreary sleep. Woke, and was ill all day, till I had galloped a few miles. Query—was it the cockles, or what I took to correct them, that caused the commotion? I think both.*

---

*Byron: Journal, February 27, 1821.

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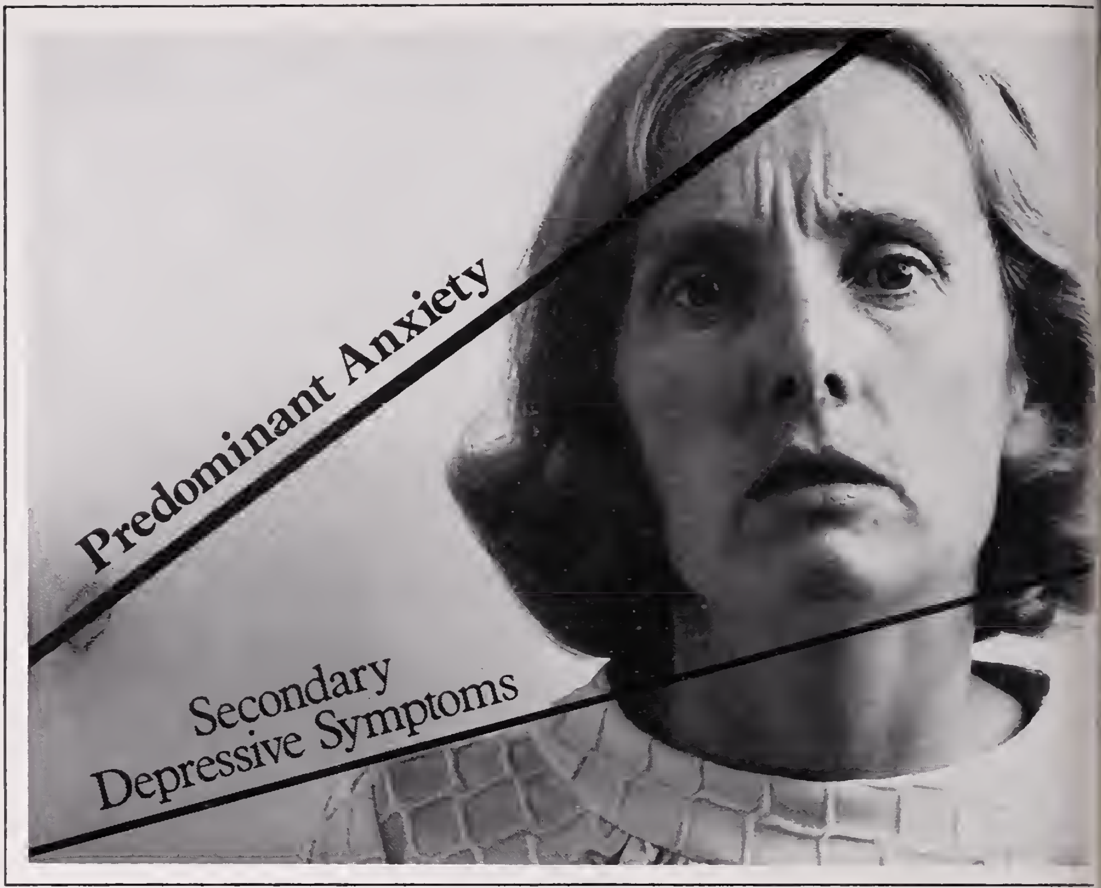

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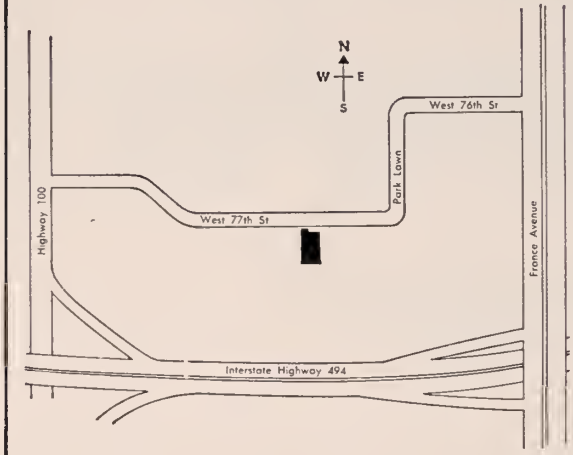

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President's Letter

Stridency

THERE IS A NASTY, carping hostility evident these days in some of the public statements of prominent figures and a stridency in what should be polite and problem-solving discussion. That mother of parliaments which since the statute of Westminster in 1275 has given us a model of respectful difference provides such examples of eloquent disagreement as William Pitt, Edmund Burke, Benjamin Disraeli, and in our time, Winston Churchill.

Why we are unable to air our differences with the gentility exhibited by these great ones of the past is difficult to determine. We tend rather to express conflict with rancor and disagreement with irascibility.

James Shannon, when he was still President of the College of St. Thomas, wrote a piece for the school paper later reprinted in several daily journals entitled, "The Tradition of Respectful Argument." He said, "One mark of an educated man is his ability to differ without becoming angry. Such a man recognizes that in contingent matters there will always be a place for legitimate difference of opinion."

Such noble sentiments are short stocked these days among the detractors of medicine. We have about us in more than plentiful supply, a host of politicians, self appointed social reformers and just plain destructive critics who point out with incomplete reasoning and distorted statistics, much that is wrong with our American system of medical care, with seemingly no recognition of the magnificant strides our profession has taken in this land. Thus, we repeatedly hear reference to neonatal mortality, life span shorter than some other country, lack of medical care in the ghetto, medical neglect of the poor and particularly we hear assertions of wildly escalating costs of care with no in depth study and no profound examination of the causes of rising costs. Just last week a prominent United States Senator said, "You (the AMA) haven't done a single thing to regulate the rising cost of medical care!" These detractors accuse with superficial study and assault with fallacious weapons and they do it in a tone which is condemnatory, petulant and at times even defamatory.

Of some comfort is that these critics are gnats compared with the geniuses of the past who have attacked our profession, Voltaire, Moliere, Diderot, Shaw. We have borne the brunt of depreciation by the geniuses of time and still our profession grows and thrives. It continues to perform every day, feats which in another century would have been considered miracles. It brings more care to more people at less overall cost than any other system of medical care ever devised by man and at the same time makes advances through research and innovation that even a few years ago would have been thought impossible. The world sends its sons to us for training and its sick for treatment and more often than not they return reluctantly to their own countries—if at all.

So our system must be defended against its detractors but not on their terms or with their rhetoric. When Edward Kennedy and Ralph Nader are long gone and quite forgotten, the names of Voltaire and Moliere will still be a shining light in the history of man's intellectual progress as will our profession. The Shaw who attacked us himself said in "The Philanderer": "The test of a man and woman's breeding is how they behave in a quarrel." Our reply to these critics and to one another should be couched in the polite deference of a profession sure of its ground and convinced of its mission. We bring our message of care first to our patients and our results to the world. We conduct our portion of debate in the spirit of Shannon, "The venerable tradition of respectful argumentation, based on evidence, conducted with courtesy and leading to a greater exposition of truth is a precious part of our heritage in this land of freedom."

John J Regan

President
Minnesota State Medical Association

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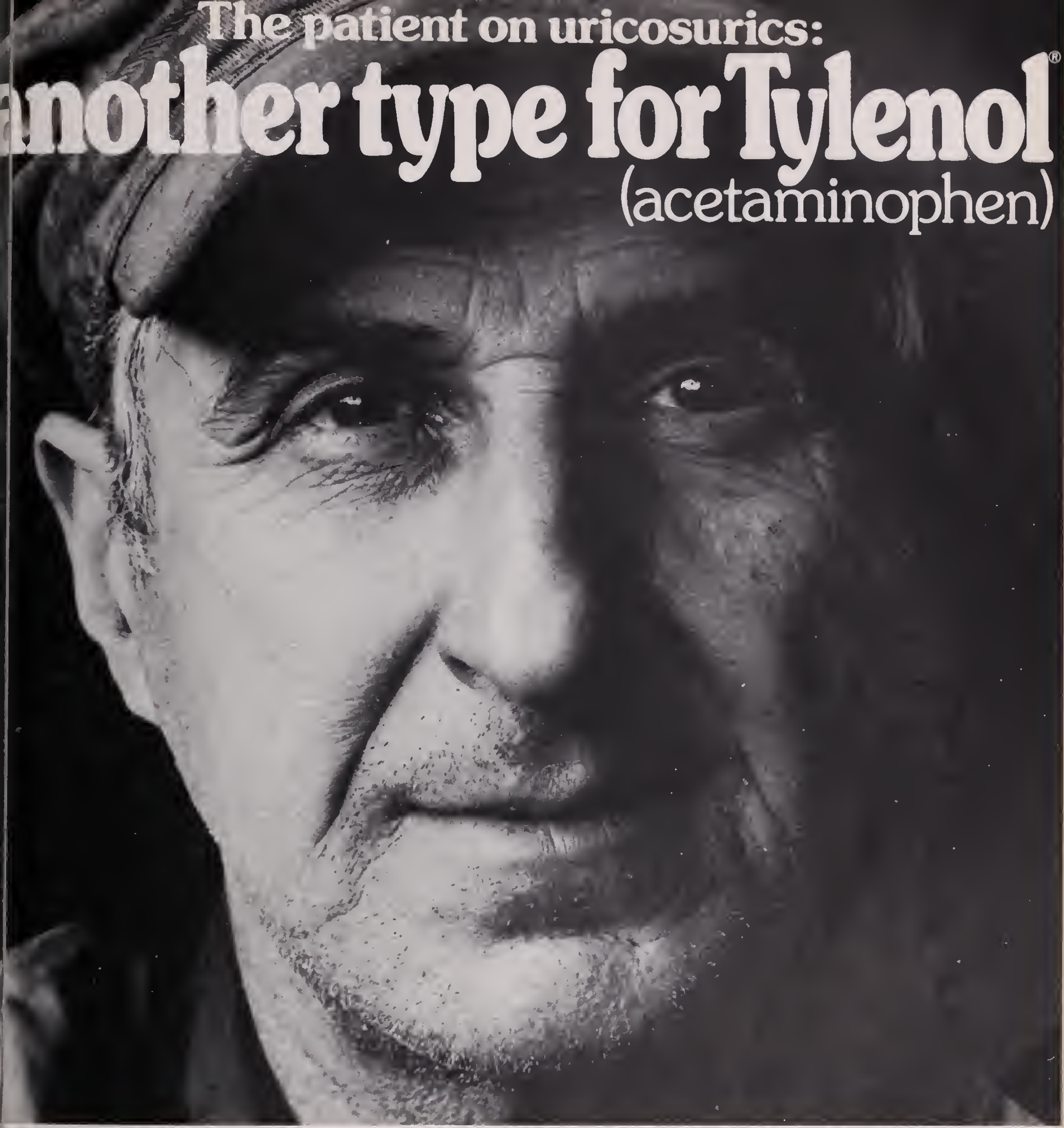

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nt Statement on Antisubstitution Laws and Regulations

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ffirm the support of the participat-
organizations for the laws, regula-
is and professional traditions which
hibit the unauthorized substitution
rug products.

Traditionally, physicians, den-
s and pharmacists have worked
peratively to serve the best inter-
s of patients. Productive coopera-
has been achieved through
tual respect as well as a common
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vice. This mutual respect has been
ected, in part, by joint support
r the years for the adoption and
orcement of laws and regulations
cifically prohibiting unauthorized
stitution and encouraging joint
cussion and selection of the
rce of supply of drug products.
basic principles of medical, den-
and pharmacy practice are thus
ized and preserved in the interest
atient welfare.

The antisubstitution laws have
obstructed enhancement of the
fessional status of pharmacy any
re than they have in and of them-
ves guaranteed absolute protec-
from unsafe drugs, or freed
sicians, dentists and pharmacists
n their responsibilities to patients.
a practical matter, however, such
s and regulations encourage inter-
fessional communications regard-
drug product selection and assure
h profession the opportunity to
rcise fully its expertise in drug
ge, to the advantage of patients.

Physicians and dentists should
urged to increase the frequency
regularity of their contacts with
armacists in selection of quality
g products, recognizing that
economies to patients can be improved through such communication, taking into account the patients' needs. The pharmacist's knowledge of the chemical characteristics of drugs, their mode of action, toxic properties and other characteristics that assist in making drug selection decisions should be utilized to the fullest extent practicable by physicians and dentists in serving their patients.

Since drug product selection entails knowledge derived from clinical experience, the physician's and dentist's roles in product selection remain primary and do not permit delegation of decisions requiring medical and dental judgments. A broader role in therapy will evolve for pharmacists as improved understanding and cooperation among the professions continue to grow.

There has been no evidence that there are convincing reasons to modify or repeal existing laws and regulations prohibiting the unauthorized substitution of another drug product for the one specified by a prescriber. It is our belief that such laws and regulations merit the joint support of the medical, dental and pharmaceutical professions and the pharmaceutical industry.

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Acupuncture Analgesia*

A Psychophysiological Explanation

R. MELZACK, Ph.D.† and MARY-ELLEN JEANS, R.N., M.Sc.A.†

Explanation of acupuncture analgesia. Research is being stimulated which will undoubtedly provide knowledge of pain mechanisms in general and new approaches to pain relief.

THE TECHNIQUE OF acupuncture, which originated in ancient China, is being used increasingly in the Orient to induce profound analgesia so that even major surgical procedures can be performed without chemical anesthetics. Over the centuries, acupuncture has been used as a form of therapy for virtually every ailment.[6] It is the more recent technique of producing surgical analgesia[1,2] that has intrigued western scientists and laymen alike. A non-chemical analgesia, particularly in the case of elderly patients, may be a valuable contribution of acupuncture. Equally important is its potential for controlling a variety of pain syndromes such as the neuralgias, causalgia or phantom-limb pain.

That acupuncture analgesia is effective in China is evident from films distributed by the Chinese Medical Association, and from first-hand observational reports by British and North American physicians who have recently visited there. They describe major operations on the abdomen, chest, and head in fully awake and alert patients who were stimulated by acupuncture needles inserted at particular points on the body. In one hospital thyroid surgery was conducted under analgesia produced by the insertion of an acupuncture needle at a point in each forearm about 20 cm above the wrist and at a depth of slightly more than 2 cm. In another hospital a similar operation was performed with acupuncture needles inserted in the neck and the backs of the wrist. E. G. Dimond,[2] an American physician who visited several hospitals in China, observed a partial gastrectomy:

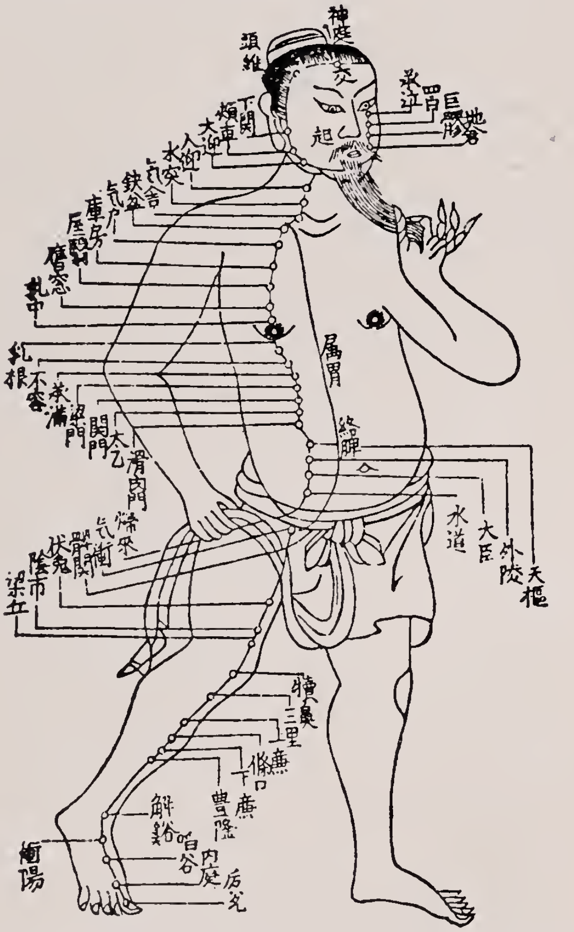

Fig. 1—A typical acupuncture chart, showing the sites for insertion of needles along one of the major body meridians. After two or more needles are inserted, electrical current is usually passed through the needles for about twenty minutes. The resulting analgesia can permit major surgery.

---

*Supported by grant No. A7891 from the National Research Council of Canada.

†Department of Psychology, McGill University, Montreal, Quebec, Canada.

See editorial, page 223.

"The patient was a slender 50-year-old man with a non-healing ulcer of the lesser curvature of the stomach. The procedure was to be a gastrectomy. This patient had not had medication at bedtime the previous night. He was given 60 mg of meperidine hydrochloride in 500 cc of 5 percent dextrose during surgery. Acupuncture anesthesia was introduced by placing four stainless steel needles in the pinna of each ear at carefully identified points . . . The needles were connected to a phasic direct-current battery source, delivering 6 volts at 150 cycles per minute. The patient remained awake, alert, and chatted throughout the procedure. A subtotal gastric resection was done by skillful surgeons, scrubbed, gowned, and disciplined thoroughly in modern or Western surgical practice. This patient required no additional anesthesia but did note some sensation associated with visceral traction."

The British physician, P. R. Brown[1] described a major operation carried out with a single acupuncture needle:

"My first introduction to this method of anesthesia was during a visit to the Cheng Hwa Hospital in Shanghai. I was taken into the theatre to see a man in his mid-thirties, who was undergoing a right upper lobectomy . . . He was fully conscious and able to speak to me. There was only one acupuncture point, situated over the right biceps muscle. A needle, 5 cm long was inserted and manually rotated by the anesthetist. She was rapidly rotating the needle for 10 to 15 seconds, at intervals of half a minute. Every five minutes she checked the pulse rate and blood pressure, and her chart revealed a steady regular pulse of 80 per minute, and blood pressure varying from 150 to 130 mm Hg systolic and from 85 to 80 diastolic . . . the patient remained extraordinarily calm. The anesthetist occasionally spoke to him in a quiet voice, and he responded immediately. I was allowed to sit with him, and ask him questions about the amount of pain or discomfort he might be feeling, but he insisted there was no pain; in fact he seemed to enjoy the segments of orange with which I fed him. He was able to chew and swallow with no difficulty. His color was good throughout, and he seldom showed any evidence of stress except when there was any traction on the trachea.

"From the surgical point of view, I noticed the extreme care taken by the surgeon and the very slow speed at which he operated. A further interesting feature was the very slight blood loss which, I was told later by the surgeon, is a major advantage of acupuncture anesthesia.

"The patient had been active during the week before the operation, and the only preoperative drug was . . . pethidine hydrochloride, administered intramuscularly. I examined him twelve hours after the operation, and he was sitting up in bed. He seemed quite comfortable, and the blood pressure and pulse were normal. I was told that the analgesic effect of acupuncture lasted for several hours after operation, and that postoperative sedation was seldom needed. The manual stimulation of the needle was given up when the wound was being sutured."

Theories of Acupuncture Analgesia

Although the technique of acupuncture is seemingly simple, the mechanisms that underlie its analgesia-producing effects present a mystery. The major properties of acupuncture analgesia defy explanation in terms of traditional Western medical doctrine. For example, there is no known mechanism to explain why somatic stimulation through acupuncture needles should produce analgesia. The fact that acupuncture stimulation at one site (such as the hand) produces analgesia at a distant site (such as the jaw) is also baffling. Equally perplexing is the fact that analgesia outlasts the period of stimulation by several hours.

Specificity Theory

Acupuncture analgesia cannot be explained in terms of the traditional specificity theory of pain.[8] Specificity theory states that specific pain receptors in the body tissues project pain signals directly through a pain transmission system to a pain center in the brain. This direct transmission line resembles a simple telephone switchboard: dial in a signal at one end and a bell rings at the other end. This means that the person will feel pain at the exact location of a damaging stimulus and further implies that pain should be blocked only by interruption of the direct-line pain pathway. This principle contradicts the observation that analgesia may be produced by stimulation at distant, seemingly unrelated sites.

Specificity theory further states that the amount of pain experienced is directly proportional to the intensity of stimulation. That an analgesic effect is produced by twirling or electrically stimulating acupuncture needles in the skin suggests that this is not necessarily the case. Acupuncture stimulation may at first be experienced as painful, yet it may also produce analgesia. It is not possible within the framework of specificity theory, to account for the analgesia elicited by acupuncture stimulation, or the observation that pain is relieved for long periods of time after the needles have been withdrawn.

Yin and Yang

The traditional Chinese theory takes quite a different approach to the explanation of acupuncture. This theory proposes that two universal forces are biologically represented in the body in the form of the spirits (Yin) and the blood (Yang). These forces flow through the body within a number of separate channels called meridians. Acupuncture points lie on these meridians or at their intersections. Traditionally, there were 365 acupuncture points falling along 12 meridians, but in recent years these numbers have varied. According to the theory, Yin and Yang may fall into disharmony, thus producing disease and pain. Somehow this harmony is restored by the insertion of acupuncture needles at specific skin sites (Figure 1).

The selection of particular acupuncture points for a specific treatment are, according to the classical Yin-Yang theory, determined by the meridians which represent different body parts and by complicated rules related to the time of day, month, and year. It seems evident that many of these sites were chosen on the basis of empirical observation. That is, the insertion of needles at certain points was discovered to have positive results in some proportion of patients. Although some of the "barefoot doctors" who practice folk medicine in the rural areas of China still adhere to the Yin-Yang theory of acupuncture, it is not so popular among physicians in major medical centers. Rather, they are currently searching for neurological explanations of acupuncture analgesia.[3,5]

An interesting claim has been made that the resistance to electrical current is different at acupuncture sites than at adjacent skin areas. Although there is still no substantial evidence on this point, if it is established as fact, it may be related to two sets of observations. First, during current investigations in our laboratories we have found a high degree of correspondence between acupuncture points and sites at which sensory and motor nerves emerge from deep tissue to more superficial levels. Second, "motor points" on the body surface, which produce localized muscular contractions when electrically stimulated, may also be related to some of these acupuncture points. Both of these possibilities would enhance maximal input to the central nervous system when these points are stimulated by twirling or electrically stimulating these inserted needles.

Hypnosis

Because the Yin-Yang theory lies outside the Western scientific approach, and specificity theory fails to explain the effects of acupuncture, many people have proposed that its analgesic effects are due to hypnosis. This hypothesis appears to be untenable on several counts.

Patients require prolonged training in hypnosis. It is reported by professional medical hypnotists that induction of a trance sufficiently deep to allow surgery requires from four to eight hours of initial training plus considerable additional time for specific instructions. This training is generally carried out over a period of several days or weeks. On the other hand, acupuncture analgesia appears to require no prior specific training as an essential aspect of the procedure. Also a trance state is usually induced as a result of a set of specific procedures, but there is no evidence that these types of procedures are employed in acupuncture analgesia.

People in a deep hypnotic trance rarely carry out normal movements or speak spontaneously without further prolonged training. Yet, patients who undergo acupuncture analgesia without any apparent training, eat oranges, sip juice, talk casually with the nurses and doctors, show interest in the operation and may even examine the excised organ or tissue. Furthermore, acupuncture analgesia can be induced in young infants and in animals, which would preclude hypnosis as a major mechanism.

The mechanism of acupuncture analgesia cannot be totally accounted for by the concept of hypnosis. This does not deny the important role of psychological factors which may substantially contribute to an adequate explanation.

Having reviewed the above hypotheses we are still left with the puzzling question: How does acupuncture analgesia work?

Major Characteristics of Acupuncture Analgesia

Let us return to the three major characteristics of acupuncture analgesia, which at first glance seem to defy Western scientific theory. These include: (a) a moderately intense stimulus, which cannot possibly block neural transmission by any known pharmacological action, nevertheless produces analgesia; (b) insertion of needles at given skin sites produces an effect at distant body parts that are not segmentally interconnected; and (c) pain is relieved for hours after stimulation has stopped. Although specificity theory has difficulty accounting for these properties, they are in fact well documented in Western medical literature.

Control of Pain by Intense Stimulation

One of the oldest methods of pain control is generally known as "counter-irritation." This method is characterized by intense stimulation on the body surface and it sometimes produces pain relief for variable periods of time. It includes such folk treatments as application of mustard plasters, ice packs, or blistering fluids.

Although these methods are still frequently used, it is only recently that any theoretical or physiological explanation for their effectiveness has been proposed. Usually, such placebo mechanisms as suggestion or distraction of attention are invoked, but neither seems adequate to account for both the power of the methods nor the long duration of pain relief which is achieved.

However, there is considerable evidence to show that brief, somewhat painful stimulation produces marked relief of more severe pathological pain for periods of time that extend far beyond the duration of stimulation.[8] For example, tic douloureux, which is characterized by painful, convulsive spasms of the face and mouth, may be permanently abolished by vigorous massage of the sensory nerve which innervates the lower head and jaw. Similarly, an injection of hypertonic saline into the interspinous tissues of the back produces a sharp brief pain which may be followed by long-term relief of phantom limb pain. This may also be achieved by saline injections into the stump itself. Experimental evidence also suggests that one pain may produce a marked rise in threshold (the lowest stimulus intensity at which pain is reported) to other types of pain. The threshold to pain produced by electrical stimulation of the teeth is raised by about 30 percent by tl application of painful cold to the shin of eith leg. Furthermore, this effect may last as long two hours. Likewise, paraplegics who suffer pa have a higher threshold to experimentally induce pain than pain-free paraplegics.

Distant Body Sites

The phenomenon of referred pain and trigg zones provides a model for examining the effec of acupuncture at distant body sites. Patients wi cardiac disease often develop referred pain in th shoulder, chest, and arm. Pressure on trigg spots in these areas frequently produces inten pain which may last for several hours. It is inte esting to note that examination of subjects wh do not suffer heart disease also reveals a simil pattern of trigger areas.[4] When moderate pressu is applied, pain may be evoked which lasts fo several minutes. The pain may actually increa in intensity for a few seconds following remov of the pressure. Similar patterns of referred pai are observed in other areas of the body.[12]

Referred pain patterns and trigger zones ar frequently used in Western medical practice fo both diagnosis and treatment. The patterns o referred pain are highly consistent from one pe son to another, as are the small trigger spots withi these areas. The application of pressure to the trigger spots evokes pain in the referred area an often in the related diseased visceral structur Injections of anesthetic drugs such as novocain may relieve both the referred pain and the pain i the viscera. A single such injection may not onl reduce the frequency of painful attacks but ma relieve it permanently.

We have found a high degree of corresponden between the various trigger areas and acupunctu spots. What is particularly fascinating is that i most cases these spots are specified in relatio to the same pathological pain patterns. Surprisin ly, physicians have also found that intense stim lation of trigger areas may abolish referred pai This usually involves dry needling of the trigg spot but may include such stimulation as the a plication of intense cold.

Central nervous system lesions also reve something of the interactions between distant bod areas.[10] Patients who have undergone anterolater spinal cordotomy, usually for relief of pain due t alignancy, report pain at some distant area uch as the chest or abdomen) when pricked by a in on an analgesic area (such as the leg). These ains can be evoked on the same or the opposite de of the body. In some cases the pain is evoked the site of an earlier injury.

ain Relief Outlasts Stimulation

Pain is relieved for varying periods of time fter acupuncture needles have been withdrawn. ctually, many pathological pain patterns inolve unusual temporal characteristics, in which rief intense stimulation may evoke prolonged ain.[8] On the other hand, a single temporary nesthetic block or a brief increase in stimulation ay abolish pains that have persisted for months r years. These phenomena suggest a much more omplex temporal relationship between stimulus nd pain than that indicated by specificity theory.

That temporal patterns of pain do not bear simple one-to-one relationship to the duration f stimulation is further substantiated by medical ecords. Referred pain may be evoked, by stimuating the tissues in the nasal sinuses, in teeth which have been drilled and filled without local nesthetic as long as 70 days prior to the stimulaion. A single injection of novocaine into the ppropriate nerve of the jaw abolishes this efect permanently. It is difficult to attribute this phenomenon to chronic local irritation due to rauma since the anesthetic block could not have ffected the teeth themselves. These observations suggest prolonged changes in central neural acivity which can be triggered by a brief, painful nput and stopped permanently by a single anesthetic block.

All of these characteristics of acupuncture analgesia, which at first glance seem magical and puzzling, are consistent with the "gate-control" theory of pain.

A Psychophysiological Explanation

The "gate-control" theory of pain, which is based on current knowledge of central neural function, suggests that the transmission of pain signals from the body to the spinal cord and brain is not a fixed, immutable process but a dynamic one capable of plasticity and modulation.[9] According to the theory (Figure 2), a gate-like mechanism exists in the pain signalling system. This gate may be opened or closed in varying degrees so that, under certain circumstances, signals from injured tissues may be blocked and fail to reach the brain. The gate control theory describes three ways by which pain can be modulated.[8]

Within somatic sensory nerves there are large and small fibers which have different effects on the transmission of pain signals. Physiological studies[13] suggest that stimulation of large fibers tend to "close the gate" and block pain signals, whereas small-fiber activity tends to "open the gate". Acupuncture stimulation, at low-intensity levels, would generally activate a greater proportion of large fibers than small fibers, thereby blocking the transmission of pain signals. The hypothesis gains support from the fact that acupuncture stimulation loses its analgesic effect if the skin sites are first injected with local anesthetic. This explanation of how acupuncture blocks pain, however, is only plausible if the needles are inserted near the painful area. It does not clarify how acupuncture needles affect distant body areas.

A second modulating mechanism of the "gate-control" theory involves the powerful inhibitory influence of portions of the brainstem over the pain-transmission system.[7,11] This inhibitory effect may operate via descending fibers which act on the spinal gating system or on fibers which project to other transmission areas in the brain. The brainstem reticular formation receives inputs

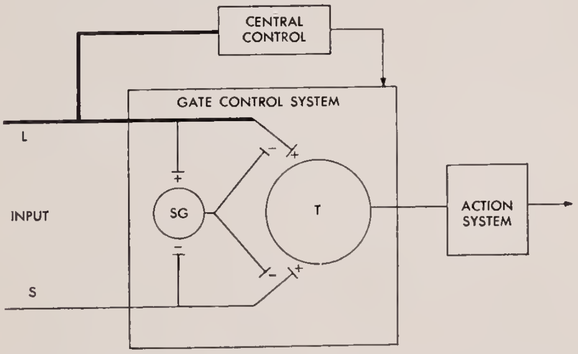

Fig. 2—Schematic diagram of the gate control theory of pain mechanisms. L, the large diameter fibers; S, the small diameter fibers. The fibers project to SG, the substantia gelatinosa, and T, the first central transmission cells. The inhibitory effect exerted by SG on the afferent fiber terminals is increased by activity in L fibers and decreased by activity in S fibers. Central control processes project to the gate control system. They include fibers from the brainstem which have a predominantly inhibitory effect, as well as fibers from the cortex. The T cells project to the entry cells of the action system. + stands for excitation; − for inhibition.[9]

from widely distributed parts of the body. Furthermore, when certain areas of the reticular formation are electrically stimulated, a profound analgesia is produced in a large part of the body. These data provide an explanation for the observation that stimulation at sites in one part of the body may produce analgesia of a distant part. In studies with rats, profound analgesia can be produced in a quarter or half of the body by electrical stimulation of certain regions of the reticular formation. These rats can be shocked, pinched or pinpricked without responding in any way that indicates pain. The duration of the analgesic effect in these studies often outlasts the period of stimulation by as long as 20 minutes. These findings suggest that the neural activities triggered by stimulation may "close the gate" for prolonged periods of time.

The third way the nervous system modulates pain perception involves descending fibers from the cortex. Psychological processes, such as expectation, anxiety, suggestion, and memory of past experiences, all have a profound effect on pain. It is well known that increased anxiety enhances pain perception while decreases in anxiety diminish the intensity of perceived pain. The important role of anxiety and fear is evident in the observation that morphine has a greater analgesic effect when pain is accompanied by anxiety, but has little analgesic effect in the non-anxious patient. The placebo effect also demonstrates the importance of these psychological processes in pain perception. Pharmacologically inert substances, such as sugar or salt, may produce post-operative pain relief in one-third of patients who believe they are receiving an analgesic. The stronger the suggestion that a given procedure will reduce pain, the more likely it will have an effect. Strong suggestion, faith in the doctor and his techniques, relaxation and distraction all contribute to the diminution of pain and anxiety. The fact that suggestion and belief in the analgesic properties of acupuncture is highly explicit in the Chinese hospital environment undoubtedly contributes to its effectiveness.

Taken together, these three modulating mechanisms of the gate-control theory provide a plausible explanation of how acupuncture analgesia works. In particular, the inhibitory effects of the brainstem reticular formation on the transmission of pain signals in the spinal cord or at higher transmission levels seem to provide a powerful explanatory concept. Intense stimulation through acupuncture needles could activate this inhibitory brainstem system, thereby closing the gate to pain signals.

We have only partial information about acupuncture. The technique is not used routinely on all patients. Which patients, then, are good candidates and which are not? Conventional pre-operative analgesic and relaxant medications are usually administered to patients undergoing acupuncture analgesia.[1] The interaction between these drugs and the actual acupuncture procedure has not been determined. Their effect, together with the faith in the procedure and the belief that no pain will be felt, which is engendered by long cultural tradition, would greatly diminish anxiety. This predisposition, then, would make it possible for the patient to feel little or no pain when the acupuncture needles are inserted and the tissues are stimulated electrically or manually. The stimulation of the needles either by twirling or mild electricity would produce nerve impulses which, in turn, would activate parts of the brainstem reticular formation. This activation would block the transmission of pain signals from the site of the surgery.

This explanation of acupuncture analgesia is based on the meager amount of knowledge we currently have available. With the increased dialogue that is developing between China and other countries we should, in the near future, have more information and a greater understanding of acupuncture analgesia. Research which is being stimulated in this field will undoubtedly provide valuable knowledge of pain mechanisms in general and new approaches to pain relief in particular.

References 1-13 are listed on page 194.

Biofeedback Techniques

Their Potential for the Control of Pain

ALAN H. ROBERTS, PH.D.*

The control of pain varies; some patients work hard to alleviate it while others earn to accept it as a way of life. There seem to be greater rewards for maintaining behaviors associated with pain than there are for alleviating it. Therefore there eems to be more than the usual potential for developing effective biofeedback or elf control procedures.

WHEN PLATO, DESCARTES, and Bichat dichotomized reason and emotion, mind and body, and the cerebrospinal and autonomic nervous systems, they provided Western medicine with basic assumptions which are only now being seriously questioned in theory, in the laboratory, and in the clinic. Plato described a "superior rational soul" n the head and an "inferior soul" in the rest of he body. Reason was associated with the voluntary responses of the skeletal muscles while emotions were related to glandular and visceral responses which were, until recently, assumed to be involuntary. Neuroanatomy makes a clear distinction between the cerebrospinal nervous system controlled by higher cortical integrated activity and the sympathetic and parasympathetic systems which are generally considered to be "inferior" and not subject to voluntary control.

Assumptions about the dichotomy of the nervous system have been paralleled in psychology by assumptions about the mechanisms of learning. Theories of learning have dichotomized classical or Pavlovian conditioning and operant or instrumental learning. The former type of learning has been considered to be involuntary and therefore also inferior. In this kind of learning a signal (termed a "conditioned stimulus") is presented to an organism along with some innate stimulus like food (termed "unconditioned stimulus"). The unconditioned stimulus is one which usually elicits some response from the organism such as salivation. If the conditioned stimulus and unconditioned stimulus are presented together enough times, the conditioned stimulus begins to elicit the response that was once stimulated by the unconditioned stimulus.

The second type, operant or instrumental learning, is subject to voluntary control and considered superior to classical conditioning. In this kind of learning a reward or reinforcement is given to the organism whenever the desired behavior occurs. In classical conditioning learning opportunities are limited because the unconditioned stimulus and the response must first occur naturally together before learning to respond to the new signal can occur. In instrumental, or trial and error, learning the reward strengthens *any* response which immediately precedes it.

Because of these differences in the two types they have been thought to be two discrete processes that involve different neurophysiological mechanisms. According to these beliefs, the inferior involuntary visceral responses of the body could be changed only by means of the inferior classical conditioning methods. The superior voluntary instrumental learning techniques, on the other hand, have been thought to be applicable only to the learning of voluntary skeletal responses.

These views have persisted despite reports of individuals who could control presumably involuntary processes like heart beat or body temperature or pain by means of meditation or hypnosis or in other ways. Reports and laboratory studies

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of these phenomena have been available in the scientific literature at least since 1885.[1] Some people can control their tears or their blushing. Neal Miller[2] points out that the urethral sphincters are largely innervated by the autonomic nervous system and yet are voluntarily controlled. Lapides, Sweet, and Lewis[3] have demonstrated that this control persists even when striated muscles are completely paralyzed by curare or succinylcholine.

There has recently been an extraordinary flurry of research demonstrating that both humans and animals can reliably learn the "voluntary" control of autonomic and other presumably involuntary functions.[4,5,6] Miller and his group first paralyzed animals with curare and then maintained them on respirators. In their experiments the animals were generally rewarded for making correct responses by means of the direct electrical stimulation of so-called "pleasure centers" of the brain. Alternatively the animals were rewarded by permitting them to escape from mild electrical shocks to the tail.

In one experiment by Miller and Banuazizi,[7] half of their animals were rewarded for changing their heart rates and half of the animals were rewarded for changing intestinal contractions. Each of these two groups of animals was further divided so that half of the animals in each group were reinforced for increases and half were reinforced for decreases in these functions. The visceral responses were first recorded accurately and small spontaneous changes in the desired direction were immediately rewarded. After small changes were learned by the animals, they were "shaped" by requiring larger changes in the correct direction before reinforcements were delivered.

In this experiment the animals reinforced for a fast heart rate learned to increase their heart rates while those reinforced for learning to decrease their heart rates did slow them down. The same findings occurred for animals rewarded for increasing or decreasing intestinal contractions. Animals trained with respect to heart rate changes did not change significantly with respect to intestinal contractions while training animals to increase or decrease intestinal contractions did not affect their heart rates.

Using similar methods, Miller and others have also taught animals to increase and decrease blood pressure, to increase and decrease urine formation, to change uterine contractions, and to control vasomotor responses. One particularly interesting finding is that curarized animals appear to learn better than animals trained without being paralyzed.[4]

Following these demonstrations that animals can learn to control normally involuntary functions through operant learning techniques, similar work has been done with human subjects. For example, Roberts, Kewman, and Macdonald[8] attached temperature measuring devices to the tips of the middle fingers of six human subjects. The subjects wore stereophonic earphones and heard a tone which moved into their left ear and went down in pitch when the left hand became warmer than their right hand. The tone moved into their right ear and went up in pitch when their right hand became warmer than their left hand. The subjects were then asked to make a specifically designated hand warmer than the other for eight minutes, reverse the temperature for eight minutes, and then reverse it once again.

Large and reliable effects were demonstrated and some subjects could change the temperature of one hand relative to the other in a predesignated direction by as much as nine degrees Centigrade. This highly specific unilateral control persisted even when the earphones were removed and the subjects no longer received the feedback of information about the relative temperatures of their two hands. Using similar methods and techniques with human subjects, it has been clearly demonstrated that electrodermal activity, heart rate, blood pressure, gross muscle potential, single motor unit activity, alpha and theta EEG rhythms, evoked cortical responses, skin temperature, and peripheral vasomotor activity can all be brought under some degree of voluntary control by some individuals.

The term "biofeedback" was coined only five years ago when the Biofeedback Research Society was formed in 1969. The topic has received extraordinary public and semi-professional attention, and spectacular reports have appeared. There are four volumes of scientific papers published.[9-12]

Biofeedback refers to any of a wide variety of techniques which use instrumentation to provide a subject with information about changes in bodily functions of which the person is usually not aware. The information provided is generally immediate nd usually continuous. When this information is rovided to the subjects, some of them use the nformation to learn to control these previously nvoluntary functions. The terms “self-control” r “self-regulation” are often used in similar conext to connote the scientific study and clinical pplication of other techniques through which a erson can control internal physiological states, nood, attention, emotions, or other normally inoluntary functions. These techniques include perant learning approaches, hypnosis, autogenic raining, and various forms and styles of meditaion. Hilgard and his group[13], Orne and his roup[14], and others have shown that hypnotic rocedures can serve as analgesics which exceed lacebo response. Fordyce[15] has demonstrated the ffective application of operant conditioning proedures to the control of behavior associated with hronic pain.

The principles of biofeedback training are imple, based upon laws of operant learning. First bodily function to be brought under control is efined and monitored with sufficient accuracy nd sensitivity to reliably detect moment to monent changes in the function. These changes must hen be translated into some information mode vhich can be fed back to the subject immediately. n humans the feedback information is usually rovided by means of a visual signal or an audiory tone. Finally, it is necessary that the subject e motivated to learn either through internal tates and attitudes such as “curiosity,” through he desire to master these functions, through a esire to use the training to alleviate physical disomfort or a medical problem, or through external ewards which may be provided by financial inentives or praise from others.

In order to comprehend how these biofeedback echniques and procedures might be applicable o the control of pain, it must be recalled that pain as both physiological and psychological comonents. Although neural pathways have been dentified for cutaneous pain, there are at least wo different systems associated with the experince of pain and they do not function in the same ashion.[16] No single pain center has been localized n the brain. *Any* intense stimulus can be experinced as painful so that specific receptors, sensory racts, and localized cortical areas are not likely o be found for pain. There are extreme individual ifferences in response to stimuli considered painul and any treatment for pain whether from drugs, acupuncture, placebo, hypnosis or electrical stimulation when administered unselectively apparently produces the identical base rates of effectiveness: one-third good relief, one-third some relief, and one-third no relief. Mood and emotional states affect response to pain and depressed individuals are likely to be more susceptible to pain than others. Depressed subjects have greater autonomic responses than do psychiatric and normal controls during (but not before or after) the presentation of aversive stimuli.[17]

Despite the inherently subjective nature of felt pain Hilgard[13] and others have shown that pain state reports can be obtained from people which are reliable, which are related to the intensity of painful stimuli in an orderly fashion, and which fit a power function with time which is consistent with standard psychophysical functions. Laboratory methods to induce pain which has characteristics similar to pains experienced clinically have also been developed. Thus, technology and methodology are now available for the scientific study of reported pain states and their relationship to other physiological and psychological states.

While no specific reliable physiological correlates of pain have yet been developed from laboratory studies, it is likely that reported pain states can be related to physiological or psychological changes which, in turn, may be brought under voluntary cognitive control. Stimuli reported to be painful can and do evoke physiological reactions such as changes in respiration, perspiration, blood pressure, heart rate, or sudden muscular contraction. State and trait anxiety, the degree of relaxation in the subject, and attentional variables all profoundly affect reported pain states. The ability to manipulate and control these variables directly by means of biofeedback training or indirectly through the training of electroencephalogram (EEG) patterns or electromyogram (EMG) muscle potential in order to produce particular mood states, change attention, control anxiety, or reduce or increase tension will determine the potential for biofeedback training in pain control.

The use of EEG feedback techniques to alter moods, change attention, or reduce anxiety have significant possibilities since mood, attentional variables, and the various forms of anxiety are all related to reported pain states. While most of the early work has concentrated upon teaching individuals to increase EEG alpha waves by biofeedback training, research on theta waves, on other newly reported high and ultra-high frequency brain waves, or on the voluntary localization of EEG productions may later prove to have greater clinical application.

However, the techniques with the greatest potential in the area of pain control are the EMG feedback procedures. These already have been shown to have some direct effects upon certain types of painful conditions such as the chronic pain related to muscle tension as well as indirect effects through relaxation and concurrent anxiety reduction.

Since autonomic processes can now be brought under voluntary control, those autonomic functions concurrent to pain states may ultimately be controlled to the point of reducing or extinguishing pain. It is possible that simply training patients in general or specific autonomic controls may permit them to control pain better. Certain individuals can inhibit pain responses through altering their state of consciousness or through simple voluntary inhibiton—two alternative explanations of hypnosis. There are suggestions in the work of Roberts, Kewman, and Macdonald[8] and others that the individuals best able to alter their conscious states through hypnosis or meditation may be the ones with the greatest facility in autonomic control and the inhibition of pain.

The most direct applications of biofeedback procedures to the control of pain use EMG feedback to alleviate the pains of tension headaches and chronic upper back and neck pains. In 1963 Basmajian[18] provided his subjects with both auditory and visual oscilloscopic feedback from an indwelling electrode and demonstrated that subjects could learn to voluntarily control the firing of individual motor units. Budzynski and Stoyva[19] developed techniques and instrumentation for training patients in deep muscle relaxation.

EMG electrodes are placed over the frontalis muscle of the forehead and their patients listen to a tone whose frequency changes in proportion to the EMG activity in the muscle. The patient is trained to decrease the frequency of the tone by relaxing the muscle group. As the patient gets better at this, instrument sensitivity is increased so that the patient must maintain lower and lower EMG levels in order to hear a low tone. The use of this technique has been reported to be effective in reducing the pain of tension headaches, and chronic upper back and neck pains. Generally the frontalis muscle is trained because it has been found that the scalp, neck, and upper body muscles tend to relax concurrently with the frontalis, but other muscle groups causing pain can be trained using these methods. The laboratory training of patients is reported to transfer to everyday life so that they become more sensitive to increasing tension and are able to reduce the tension thus alleviating the painful symptoms apparently associated with it.

Gessel and Alderman[20] attempted to treat the pain of myofascial pain syndrome using relaxation training without instrumentation. This disorder involves pain around the jaw and sometimes the ear with muscle tenderness sometimes extending as far as the neck, shoulders, arms, and even the forearms. Bruxism (grinding teeth) is very commonly associated with this disorder. Six of their eleven patients reported significant improvement following muscle relaxation training and it would seem that biofeedback instrumentation would work as effectively or better with greater efficiency.

The bruxism which is believed to be etiologically related to this problem tends not to occur when patients sleep on their backs. James Butler of the University of Minnesota Dental School is presently experimenting with a feedback device which signals patients when they attempt to turn over in their sleep thereby preventing bruxism.

For the pain of migraine headaches, a more complicated type of biofeedback procedure is being experimented with. Elmer Green and his colleagues at the Menninger Clinic[21] have evidence that some patients can learn to abort migraine headaches by learning to lower the temperature of their foreheads relative to their hands. Temperature measures are made of the fingertips and changes in skin temperature (reflecting changes in blood flow) are visually monitored by the patient. Those patients who were able to voluntarily increase blood flow to the hands generally report pain relief. These experimenters hypothesize that changing blood flow to the hands simultaneously alters blood flow to the head thus interfering with the vasodilation associated with migraine pain. It is, however, possible that training patients to master any autonomic function might make it easier for them to control their headaches. Placebo effects would also have to be ruled out. The Menninger group report improvement in 12 out of 15 migraine patients they have worked with thus far.

Another approach to the biofeedback control of pain is reported by Gannon and Sternbach.[22] They noted that certain skilled meditators have been observed to emit large amounts of alpha waves and no alpha blocking when monitored by EEG recording while simultaneously showing dereased reactivity to pain. Using the biofeedback echniques originally developed by Joe Kamiya[6] hey trained one patient with recurrent and inractable headache pain to increase alpha at will. They report that the patient learned to prevent he onset of pain by means of the operant alpha onditioning techniques they used.

Similar studies are being conducted by Melzack[23] and by Weinstock.[24] Weinstock uses a combination of EMG feedback, thermal biofeedback raining, self-hypnosis, and training of the patient o make alternative responses to stressful situaions. He reports a series of seven patients "pain ree" after using this approach. Melzack uses a ombination of alpha EEG feedback and hypnosis and reports significant pain relief for preliminary work with three patients.

The applications of biofeedback and self-control techniques to the treatment of pain and painful disorders are in primitive stages of development. While it seems likely that most individuals can learn some degree of voluntary control over normally involuntary functions when biofeedback techniques are properly applied, there are large individual differences among subjects so that only a few seem able to learn or maintain enough control for clinical application. The procedures involved are time consuming and expensive and it has yet to be demonstrated that any of them can be successfully applied to any single disorder.

Because pain hurts, there is usually great motivation on the part of the patient to work hard to alleviate it. For other chronic pain patients pain becomes a way of life and there are greater rewards for maintaining behaviors associated with pain than there are for alleviating it. The techniques described in this paper generally require a high degree of motivation. But because the paths to pain control are so variable there seems to be more than the usual potential for developing effective biofeedback or self-control procedures.

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Minnesota State Medical Association

121st Annual Meeting of the Minnesota State Medical Association will be held in Duluth, May 16 and 17, in the Duluth Arena-Auditorium.

Percutaneous Local Electrical Analgesia

Origin, Mechanisms, and Clinical Potential

ARTHUR TAUB, M.D., Ph.D.*

Percutaneous local electrical analgesia will likely find its usefulness in the induction of conduction blockade in selected peripheral nerves without the side effects of local anesthetic agents.

Electrical stimulation of peripheral nerves for the control of pain has a relatively brief history. In the early 1960's, Shelden,[1] using chronically implanted electrodes, stimulated the region of the trigeminal ganglion in man in an effort to suppress the pain of trigeminal neuralgia. He believed that prolonged depolarization of the terminals of primary trigeminal nerve fibers would restore normal function. Shelden and his associates[2] reported three patients in whom stimulating electrodes had been implanted in the region of the mandibular division. In only one patient did they actually activate the electrodes, as the other two obtained relief from the implantation procedure alone, which can be expected when the region of the gasserian ganglion is subjected to almost any trauma.[3] In the patient in whom the electrodes had been activated, hypalgesia and hypesthesia were experienced in the mandibular division during stimulation. The pain of trigeminal neuralgia was reported to have been relieved.

Another approach began in 1959, when Noordenbos[4] suggested that impulses arriving into the central nervous system over large myelinated primary afferent nerve fibers exerted a modulating influence over impulses arriving later over the more slowly conducting smaller myelinated and unmyelinated primary afferent fibers. He felt that there were pathological states in which large myelinated fibers were relatively deficient in the peripheral nerve, such as, for example, in postherpetic neuralgia. In these states the action of the smaller myelinated and unmyelinated fibers would take place unhindered, and pain would be produced even with non-noxious stimulation of the skin. Smaller myelinated and unmyelinated fibers were believed primarily to conduct impulses derived from nociceptors, since inclusion of the smaller myelinated, or A-delta, or the unmyelinated, or C fibers, in the afferent volley produced by electrical stimulation produced pain in man.[5]

These ideas, and previous studies in experimental animals,[6] prompted physiologists to search for single fibers within the smaller peripheral nerve fiber group which could respond to stimulation of nociceptors in the skin. This search remained unproductive for almost a decade, for purely technical reasons. The early studies seemed to show that very few peripheral nerve fibers conducted impulses from peripheral nociceptors. Fibers within the smaller sized portion of the primary afferent spectrum were found to respond to light tactile and to thermal, but rarely to noxious stimuli.[7,8,9] This was "paradoxical" and it seemed important at the time to develop a theory which could explain how the electrical stimulation of smaller peripheral nerve fibers could produce pain, even though their receptors apparently responded to the same stimuli as

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did larger fibers, whose activity, apparently, could suppress pain.

The "Gate Control" Hypothesis

The "gate control" hypothesis was thus elaborated by Melzack and Wall.[10] In essence, following Noordenbos,[4] it postulated that sensory mechanisms were controlled by a negative feedback mechanism activated by large myelinated fibers. The activity of smaller peripheral afferent fibers inhibited those cells in the spinal cord which generated the negative feedback.[11] It was thought that the smaller peripheral afferents were relatively incapable of producing reflex or ascending afferent effects on their own, and thus, that their function was, in the language of electronics, to "gate" the action of the larger myelinated fibers. That is, activation of small myelinated fibers permitted the effects produced by large myelinated fibers to occur. These effects included ascending and reflex activity, in addition to negative feedback. The sum of the action of large fibers upon certain "T", or transmission, cells ultimately produced pain. The "gate control" theory was attractive in many respects, not the least of which was in the attempt to explain phenomena of dysesthesia produced by tactile stimuli. This would occur whenever larger myelinated fibers were relatively decreased in number in peripheral nerve, thus reducing negative feedback. Conversely, when large myelinated fiber activity predominated in a peripheral nerve, input, otherwise resulting in pain, would be counteracted by negative feedback.

Clinical Experience

With the "gate control" hypothesis as background, Wall and Sweet,[12] using implanted electrodes, electrically stimulated the peripheral nerves of patients with a variety of localized chronic pain syndromes. They reported temporary relief of pain, outlasting the stimulus, occasionally by hours. The major sensation reported during the electrical stimulation was one of vibration. From this latter observation, it was inferred that only larger myelinated fibers had been stimulated, an observation consistent with the predictions of the "gate control" hypothesis. In a further report on the procedure by Sweet and Wepsic[13] it was noted that other sensations, including burning discomfort, were experienced during the application of the counterstimulus. In the discussion of this report, it was pointed out by O'Leary[14] that such sensations implied that smaller peripheral afferents had also been stimulated, and thus the mechanism of action of the procedure was far from being a clear-cut hyperactivation of large myelinated fibers. No action potential data were obtained from the peripheral nerves stimulated and no decision as to the mechanism of the effect could be made. Nevertheless, the notion that the activation of large myelinated fibers alone could produce clinical analgesia developed from these observations. Meyer and Fields[15] reported observations similar to those of Wall and Sweet,[12] with similar inferences, and without action potential data, in a series of patients with "causalgia", whose peripheral nerves were stimulated percutaneously.

As a result of these and other observations, a number of manufacturers of electronic devices have now produced instruments capable of stimulating peripheral nerves through the skin, or of directly stimulating them via cuff electrodes. While the latter instruments are somewhat sophisticated in design, and use radio-frequency instrumentation similar to that used in cardiac pacemakers, the former are little different in principle from a number of electrical stimulating devices long used by nonmedical practitioners. As these instruments and techniques begin to be used to try to alleviate pain, it becomes important to determine the precise neurophysiological mechanism of action of percutaneous stimulation of peripheral nerves in controlling sensation and in induction of local analgesia.

Neurophysiological Mechanism of Percutaneous Local Electrical Analgesia

The more recent development of peripheral nerve stimulation for control of pain arose from the idea that whatever effect was observed depended primarily upon *central* nervous system mechanisms; that is to say, that the centrally inhibiting spinal cord "gate" was activated by stimulation of large myelinated peripheral nerve fibers, which fibers, as pointed out above, were inferred to have been stimulated alone because of the vibratory sensation experienced by the patients and experimental subjects. This assumption turns out to have been incorrect.[16] It was made in the absence of action potential data, and precisely what portion of the fiber size spectrum was required to be stimulated for hypalgesia to be induced was not studied directly.

When a pair of circular stimulating electrodes is placed upon the proximal phalanx of the index finger, and the finger is stimulated with square wave electrical stimuli, 0.1 msec duration, at 100 Hz, with the stimulating voltage slowly increasing, a repeatable sequence of phenomena occurs.[16,17] With increasing voltage, a threshold value is attained at which a sensation of vibration is felt, projected throughout the entire finger and into the fingertip. As the stimulating voltage is raised, this sensation becomes more intense. If the threshold for perception of a tactile stimulus at the fingertip is now tested, it is seen to have risen. The threshold for discrimination of the sharpness of a pin remains unchanged. If the compound action potential of the median nerve, as derived from stimulation of the finger, is recorded at the wrist, through the intact skin, with the aid of a signal averaging computer, it is seen that only the larger myelinated primary afferent fibers have been stimulated. As the stimulus intensity is further increased, a level is reached at which a bright, uncomfortable, dysesthesia is felt, again projected to the fingertip. At this point the compound action potential reveals that the smaller myelinated primary afferent fibers have been stimulated. The dysesthetic sensation is very brief, a matter of seconds, and the compound action potential reflects this brevity by showing the disappearance of the wave representing the smaller myelinated fibers. Increasing the stimulus intensity further produces a brief dysesthesia with each increment of voltage, followed by rapid adaptation of the sensation. When a stimulus intensity of approximately 30 volts is reached, the finger is noted to be insensitive to tactile stimuli, and a pin is felt not at all, unless it is actually thrust through the skin, in which case it is not particularly painful. The action potential of the smaller myelinated fibers is seen to be gone from the compound action potential record, and some depression of the action potential of the larger myelinated fibers is also present. Anesthesia of the fingertip does not occur until smaller myelinated fibers are *stimulated* and have *adapted* to the stimulus. The postulated inhibitory effect of stimulation of larger myelinated fibers alone is not sufficient for anesthesia. If the tactile and pin thresholds are tested proximal to the electrical stimulus, or in other fingers of the same hand, no noticeable change occurs, in contrast to the predictions of the "gate control" hypothesis, and suggesting instead that an inactivation of conduction of smaller myelinated fibers has occurred. This is demonstrated directly in another experiment. If, replacing a pin, a second pair of electrodes is placed on the distal phalanx of the index finger and activated simultaneously with the "blocking" stimulus, it is seen that impulses are not recordable beyond the proximal phalanx.[18] If the "blocking" stimulus is removed, the finger gradually regains its sensitivity to pinprick, and fiber conduction is restored in about an hour.

These data indicate that percutaneous local electrical analgesia is produced by blockade of primary afferent fibers, and probably not by "gating" effects. The phenomenon, the "fatigue" of peripheral nerve fibers by higher frequency electrical stimulation, is not absolutely novel, having been described in experimental animals by Bishop.[19] Blockade of the myelinated fiber system was produced by a similar means by Collins et al.[5] in their study of the effects of unmyelinated fibers in man. What is new is the demonstration that this effect can be utilized experimentally in man for brief analgesia and anesthesia.

Clinical Promise

It is of course of the greatest interest to enquire as to whether this technique can be utilized for long term, reversible, analgesia. The phenomena described are similar to those experienced when conduction in peripheral nerves has been blocked by the application of a compressive force or by a brief percussive injury. Although conduction is eliminated for long periods of time, Wallerian degeneration does not occur.[20] This effect, in man, is called neuronapraxia. The longest time, in these studies thus far, in which the blocking stimulus for percutaneous local electrical analgesia has been applied is about one-half hour, and all effects have been completely reversible. Studies of application of the electrical stimulus for longer periods of time, which involves the risk of possible permanent nerve damage, should await the results of preliminary studies now underway in experimental animals.

It appears likely that percutaneous local electrical analgesia will find its immediate usefulness in the induction of conduction blockade in selected peripheral nerves, without the side effects of local anesthetic agents. When the appropriate protocols are complete, it will be possible to discern what side effects, if any, are introduced by this procedure.

Role of the "Gate Control" Hypothesis

What, then, is the role of the "gate control" hypothesis at the present time in a reasonable formulation of pain mechanisms? Since the time of its original construction considerable investigation into the assumptions and implications of the "gate control" hypothesis has taken place, and much has been brought forth contradicting them, and obviating the necessity for the theory. For example, information has accumulated showing that the smaller fibers in the peripheral fiber spectrum are provided with nociceptors,[21] that they interact with specific cell layers[22,23,24,25] within the dorsal horn of the spinal cord concerned with nociception, and that they have much more than a "gating" function. These facts, unknown at the time the "gate control" hypothesis was constructed, make it less urgent to invoke a complex balance of the influence of fiber sizes to explain the phenomena of pain. The fundamental experimental observation of the theory, the specific inhibition by smaller fibers of spinal cord negative feedback mechanisms, has been disputed in detail.[26] Nevertheless, the "gate control" hypothesis serves to focus overall attention upon possible mechanisms for inhibition of afferent input at spinal cord and higher levels. Some of these mechanisms had previously been demonstrated at thalamic and cortical levels,[27] and at spinal levels.[28] The existence of central inhibitory effects in experimental animals should prompt further cautious study to determine their clinical usefulness in man. This, however, should logically follow upon maximum exploitation of peripheral mechanisms not requiring central nervous system surgery or electrode implantation.

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Treating Pain with Drugs

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The use of potent narcotics to control severe pain should be limited to acute diseases or to patients with inoperable or recurring cancer who require chronic relief. Prolonged use of narcotics in patients with benign disease is proscribed because of serious side effects, addiction liability, and the development of tolerance. Long-term use of analgesic drugs in chronic pain usually produces more negative behavioral complications than the pain relief it was desired to eliminate.

SYSTEMIC ADMINISTRATION of analgesics and other drugs is the most common method of managing pain. Analgesics act on the central nervous system to interfere with the development of negative affective responses, thus reducing or abolishing the perception of pain and produce these effects without necessarily producing unconsciousness. Other types of drugs are useful singly or in combination with analgesics insofar as they can decrease fear, anxiety and apprehension; reverse depression, promote sleep or reverse psychotic pain. Since analgesics are palliative agents, agents with specific therapeutic action are usually administered simultaneously. When properly administered analgesics are effective and have significant advantages in simplicity of administration and low cost, over many other procedures. Unfortunately, these desirable qualities are frequently responsible for imprecise application due to the incorrect choice of drug, wrong dosage or over- or under-use.

Basic Considerations

In approaching drug selection, physicians must differentiate disorders that are primarily traumatic (a burn or broken bone), pathophysiologic (infection or inflammation), or psychologic (perceptive or affective disorders, neuroses, and psychoses). When a significant psychologic factor is evident, or when pain complaints persist without sufficient demonstrable cause, treatment of psychological problems in relation to pain behavior becomes paramount. Affective changes induced by continuous administration of opiate or sedative hypnotic medications over many years should not be overlooked. The patient's continuing complaints about "pain" may be veiled requests for analgesics, sedative-hypnotics, or minor tranquilizers or for narcotic analgesics to support a drug dependence of which the patient may not be aware. Narcotic analgesics may partially compensate a patient; withdrawal of sedative hypnotics, minor tranquilizers, or opiates, may revea longstanding psychoses or neurotic behavior.

Analgesic drugs can be divided into non-addictive, moderately addictive, or strongly addictive agents. The choice of an optimal agent for specific problems requires consideration of a variety o factors, the most important of which are quality intensity, duration, and distribution of pain. The non-narcotic or antipyretic analgesics may be useful in the control of mild pain such as headache, joint pain, neuralgias, and myalgias. Some are especially effective when the treatment o rheumatic disorders is considered. When administered alone these compounds are usually no effective in controlling moderate or severe pain and are not generally useful in managing pain arising from spasm of smooth muscle. As the intensity of pain increases, the use of codeine or other agents of relatively low addiction potential alone or in combination with non-narcotic analgesics may be beneficial.

Severe pain usually requires therapy other than simple analgesic medication. Strongly addictive drugs are useful only when non-addictive drugs are ineffective and other forms of pain management cannot be used or are only partially effective. Early use of strong analgesic drugs should be avoided as too early administration may mask ymptoms and make diagnosis difficult during heir duration of action. The narcotic analgesics re all strongly addictive, i.e., associated with he development of tolerance and physical dependence, but are considerably more effective han weak or non-addicting agents. They are seful for pain associated with burns, trauma, deep structures, and musculoskeletal disorders. ntense pain as in coronary occlusion, acute pancreatitis, biliary or renal colic, often requires hese potent narcotics.

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Once an analgesic drug has been selected for se in a particular patient it is necessary to determine optimal dosage. Optimal dosage may be defined as the minimal dose repeated often enough o produce the desired therapeutic effect while voiding complicating side effects. Implicit in he selection of optimal dosage is continued obervation of the patient in order to properly valuate pain relief and to discover undesirable ide effects early. Proper evaluation of analgesic herapy may require the help of the patient's amily and attending nurses.

An unfortunate but widespread practice is that of prescribing analgesic drugs and assuming without proper follow-up that patients derive relief, because the amount and type of medication were described as adequate in the manufacturer's package insert. Therapeutic failures with analgesics may occur not because the patient is hypersensiive, has an idiosyncratic ability to fail to respond o the drug, or is psychoneurotic, but because he drugs and dosages chosen by the physician are inadequate for the job at hand.

The Non-Addictive Agents

The non-addictive agents include the salicylates, salicylamide, the aniline derivatives, the phenylpyrazoles, mefenamic acid (Ponstel) and indomethacin (Indocin). In clinically useful dosages, hese agents are without psychotropic activity, except for changes in affective behavior concomtant with relief of fever, inflammation, and pain. Although these drugs are widely abused, long-erm use is not associated with the development of physical dependence and tolerance. Psychologcal dependence is not unknown and is reinforced by frequent advertising which extols the virtues of buffered or unbuffered, soluble, effervescent, and insoluble products. The mechanisms by which hese drugs produce analgesia is largely unknown, but evidence exists that they act peripherally on pain perception, for instance by blocking the generation of impulses at chemoreceptor sites for pain in skin. The great variety and over-the-counter availability of non-addictive analgesic agents and the great volume of television promotional (at times quite misleading) advertising continue to confuse the public (and even physicians) about the properties of aspirin and other salicylates. Since these agents can be obtained without prescription, toxicity often results. Patients may be reluctant to accept these agents when prescribed for a specific indication because familiarity has bred contempt.

Acetylsalicylic Acid (Aspirin)

Aspirin is the most frequently used and the most effective analgesic. It is as effective as, and cheaper than, proprietary drugs and has a relatively low incidence of side effects at doses in the range normally used. Aspirin continues to be the standard of comparison for new drugs for the relief of mild to moderate pain. Physicians should consider the use of a new drug in this class only if its performance is equal to or greater than aspirin's analgesic efficacy, while maintaining aspirin's low incidence of side effects. Controlled studies with patients in pain from varying causes have repeatedly shown that analgesia produced by aspirin in doses of 0.3 to 0.6 grams every four hours is superior to that produced by placebo medication.[3,4] Doses exceeding 0.6 grams apparently produce no increase in peak analgesia but may prolong the analgesic action. Increased side effects occur as doses are elevated over 0.6 grams but the risk may be justified when aspirin is used for its antirheumatic properties. Administration of higher doses is questionable when the drug is used for its analgesic properties alone in nonrheumatic pain problems. Following oral ingestion salicylates are absorbed in the stomach and upper intestine, resulting in appreciable plasma concentrations in 30 minutes or less with peak concentrations at about two hours. Despite widely publicized claims of one brand of aspirin reaching peak plasma levels quicker than others, there is little evidence equating pain relief with salicylate plasma levels. Salicylates are absorbed by passive diffusion of the non-dissociated lipid soluble molecule. The gastric mucosa at acid pH favors absorption by increasing concentration of the non-ionized form, but at the same time it decreases the solubility of solid tablets. Net absorption therefore, is a result of the rate of dissolution of the tablet, the amount of non-ionized drug present at the gastric mucosa, and the gastric emptying time. Chronic use of aspirin or the use of large dosages may produce epigastric distress and sometimes painless gastrointestinal bleeding, especially in patients with peptic ulcer. Sensitivity to aspirin often appears in patients with asthma and allergy. Excessive dosages produce salicylism consisting of tinnitus, headache and other mild mental effects, sweating, gastrointestinal disturbance, tachycardia, and tachypnea. These symptoms may progress to stupor, hyperthermia, hyperventilation, and changes in acid-base and electrolyte balance leading to coma, cardiovascular collapse, respiratory failure, and death.

Special Aspirin Preparations

There is poor correlation between blood salicylate levels and analgesic effects. This has led to numerous attempts to modify the absorption and elimination of aspirin to produce earlier, greater or more prolonged analgesia. Most of the studies comparing special aspirin formulations or other salicylates with aspirin have assayed blood salicylate levels only, instead of the overall analgesic effectiveness compared to blood salicylate levels as would be required to make a valid comparison.[11,12] Blood salicylate levels unfortunately do not correlate well with analgesic effectiveness particularly when simple salicylates are compared with aspirin based mixtures.[3]

Comparison of plain aspirin with special aspirin preparations may also be confused by the crucial factor of bioavailability of drug. Different preparations of aspirin may vary in the rate at which they deliver the drug in biologically useful form. This variability is further compounded by several factors: what physical state the tablet is in when it arrives in the stomach, whether the tablet was administered with or without water, whether the tablet was chewed or swallowed, or had been dissolved in effervescent solution, how much food was present in the stomach and whether salicylate was administered in an alkaline medium. Aspirin dissolved in water or in water containing alkali tends to increase blood levels of unhydrolyzed aspirin as well as total salicylate; however, the presence of excess alkali and repeated administration of effervescent preparation may alkalinize the urine and cause an increase in salicylate clearance, decreasing plasma salicylate levels.

Buffered Aspirin

Mixtures of aspirin and antacids were developed in attempts to enhance absorption and produce more rapid analgesia. TV promotional material for buffered aspirin claims that it acts faster than regular aspirin and induces less stomach irritation, but clinical evidence is not very convincing that it has a more rapid onset, greater peak analgesic action or prolonged duration of analgesia than that of ordinary aspirin.[1,2,5] Calcium carb-aspirin (Calurin) which is the most soluble acetyl ester of salicylic acid is said to be more rapidly absorbed than aspirin, however, again, a well-controlled clinical study has not substantiated these claims. These results are not unexpected in view of the aforementioned factors of the influence of absorption and analgesic po-

TABLE 1

Analgesics and Other Drugs for Relief of Pain

Mechanisms of Interference With Pain	Drug Type
Reversal of specific pathophysiologic events, such as:	
Infection	Antibiotics
Inflammation	Anti-inflammatory agents
Gout	Antihyperuricemic agents
Interference with specific chemical substance involved in pain reception peripherally	Antipyretic analgesics
Interference with conduction of pain away from affected site	Local anesthetics
Interference with central nervous system perception of pain and development of affective responses	Narcotic analgesics
Interference with anxiety, tension or depression	Sedatives and hypnotics Phenothiazine tranquilizers Skeletal muscle relaxants Antidepressants
Interfence with consciousness	Anesthetics

ency and because of overall difficulty in clinically ssessing potency and analgesic responses to this lass of agents.

nteric Coated Aspirin

This form of aspirin was introduced to prevent r reduce gastric irritation by delaying absorp- on of the drug until it reaches small intestine iereby preventing corrosive effects of salicylate rystals on gastric mucosa.[15] Great differences in ates at which these tablets pass through the tomach and are absorbed in small intestine cause ariable and at times unpredictable analgesic ction.

ustained Release Aspirin

This type of aspirin was formulated to in- rease the duration of pain relief, however, su- eriority over standard aspirin preparations ad- ninistered repeatedly has not been adequately emonstrated.

spirin Compounds

Mixtures containing aspirin, phenacetin, and affeine have long been popular because these rugs are thought to produce greater analgesia han aspirin alone. No data exist which impres- ively describes superiority or inferiority of APC ype compounds to aspirin in the majority of pa- ients with pain. This is surprising when compared ith the popularity of this group of drugs.

ther Salicylates

Sodium salicylate and choline salicylate (Ar- hropan) are more soluble than aspirin and the- retically should act more rapidly, however clini- al trials have shown that they produce less atisfactory analgesia than aspirin and thereby ave limited utility. Salicylamide, which was syn- hesized over a hundred years ago, recently has een advocated as a substitute for aspirin in atients with rheumatic fever and as an ingredient n analgesic mixtures. The analgesic and anti- heumatic properties of this compound are not asily demonstrated even after dosages high nough to produce gastrointestinal and central ervous system side effects. In patients with noderate or severe pain the drug does not seem o be more effective than placebo medication.[2] lthough salicylamide can be used safely in pa- ients who are allergic to aspirin, other aspirin substitutes are probably more effective. At present there seems to be little to support the use of this agent.

Para-aminophenols (phenacetin, acetophenetidin) are often used as substitutes in patients who are allergic to salicylates or for some reason are unable to tolerate these compounds. The usual dose is 0.3-0.6 gm every three to four hours. Phenacetin is found in many headache powders sold without prescription and for this reason, tends to be frequently misused. Toxicity occurs from ingestion of large amounts over long periods and manifests as methemoglobinemia and sulfhemoglobinemia which cause cyanosis, dyspnea, weakness, and anginal pain. Evidence suggests that phenacetin is comparable in potency to aspirin as an analgesic but may be somewhat less potent as an antipyretic.[11]

In a few instances hemolytic anemia has been attributed to the use of phenacetin.[6,8] This anemia may appear in chronic, mild form after use of large doses of phenacetin, and seems to disappear on discontinuation of the drug. More rarely, acute severe hemolytic anemia may occur after a single dose of phenacetin in individuals with an inborn glucose-6-phosphate dehydrogenase abnormality. Even more rarely, the same reaction may occur as an allergy. Phenacetin does not appear to cause gastric blood loss in a manner similar to that of aspirin. A rare sensitivity reaction is skin rash. Many recent reports have linked excessive consumption of phenacetin-containing analgesics with renal papillary necrosis,[10] however, incontrovertible evidence that phenacetin causes nephropathy is lacking. Nonetheless, many clinicians have discontinued the use of phenacetin and phenacetin-containing compounds.

Acetaminophen has been reintroduced as a substitute for phenacetin because of the reduced incidence of methemoglobinemia and other toxic reactions. The usual dose of this compound is 0.3-0.6 gm every three to four hours. Renal damage following the use of acetaminophen has not been reported nor is this compound thought to cause gastrointestinal hemorrhage. Acetaminophen therefore is recommended as a long-term substitute for aspirin when the latter is contraindicated. The compound is approximately equipotent with aspirin as an analgesic and antipyretic, however, it is decidedly less effective than aspirin in rheumatoid arthritis and other inflammatory conditions.

Pyrazolones

Aminopyrine, a highly effective analgesic, antipyretic and antirheumatic drug, has a relatively high risk of agranulocytosis, making its routine use for chronic pain unjustifiable. Phenylbutazone (Azolid, or Butazolidin), a congener of aminopyrine, relieves pain primarily by anti-inflammatory action. The dosage varies, but 0.4 to 0.6 gm daily in three divided doses produces maximum benefit. The risk of toxicity is the same as that of aminopyrine; therefore, the drug should be restricted to short-term use, not longer than one week for treating acute tendinitis, bursitis and gout, and for tiding over patients with rheumatoid arthritis. In patients with rheumatoid spondylitis, phenylbutazone has provided effective maintenance in dosages of 0.1-0.2 gm daily, less than half the amount needed for other conditions without toxicity. Oxyphenbutazone (Oxalid, Tandearil), a metabolite of phenylbutazone was introduced as a compound having approximately equianalgesic efficacy as, but less toxicity than, the parent compound. Unfortunately, this has not proved to be the case. The usual daily dosage of this compound is 0.3-0.4 gm divided into three or four doses. The patients receiving phenylbutazone or oxyphenbutazone must be closely monitored with frequent hemotologic studies to properly determine the occurrence of serious side effects, necessitating discontinuation of the agent. Because of the possibility of serious adverse effects and lack of good evidence indicating superior analgesic potency, pyrazolones are rarely if ever indicated for general purpose use in relief of pain.

Indomethacin (Indocin)

In terms of the analgesia produced in nonrheumatic pain, 50 mg of indomethacin has been found to be approximately comparable to 600 mg of aspirin. However, indomethacin is recommended exclusively as an anti-inflammatory agent in rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, and acute gout. Chronic administration of this drug should be limited because of the substantial incidence of adverse effects on the central nervous system and the gastrointestinal tract; it should not therefore be used as a general purpose analgesic. In treatment of rheumatoid arthritis, its intended purpose, results have bee disappointing. The drug has been found to b more effective than salicylates in relieving pai of osteoarthrosis of the hip and other periphera joints, acute gouty attacks, spinal osteoarthriti and rheumatoid spondylitis. Patients should b started on 50-75 mg per day and dosages increase until side effects appear.

Carbamazepine (Tegretol)

Carbamazepine represents a major advance i the treatment of trigeminal neuralgia, glossopharyngeal neuralgia, and other central pain. Th usual starting dose is 100 mg twice daily unt relief is achieved, but in no case should muc more than a gram be given daily. The drug i not useful for relieving other types of pain an carries a small risk of serious hematopoietic sid effects, therefore it should be used for the centra pain states described above and the patient shoul be examined frequently for side effects. In patients who do not tolerate carbamazepine ver well, diphenylhydantoin (Dilantin) may reliev the pain of tic doloreux and other central pai states.

Weak Narcotic Agents with Low Addiction Potential

Codeine

If one excludes aspirin, codeine is the mos widely used oral analgesic and is generally accepted as the standard of comparison for th drugs in its category. Prolonged use of codein in the dosage of 65 mg or more every four t six hours for several months is associated wit relatively little risk of significant narcotics dependence. Tolerance does develop, however, requiring an increase in dosage to provide continuing relief. The incidence of codeine abus among addicts is relatively small as is the incidenc of serious side effects from the drug. The lo incidence of abuse should be contrasted with th frequent use and easy availability of the drug t dispel addiction-abuse fears.

Codeine is capable of producing all the adverse effects characteristic of narcotic analgesi drugs, including nausea, vomiting, sedation, an dizziness; these effects being more often observe in ambulatory patients than those confined t bed. Although 60 mg of codeine can measurabl depress respiration, the degree of depression i f little clinical significance. The relatively small icidence of serious side effects together with ow cost makes codeine superior to other analesics with low addiction potential. This drug is ecommended in preference to new, relatively ntested analgesics for treatment of moderate ain that shows minimal response to non-addicve drugs.

ropoxyphene (Darvon)

Propoxyphene has enjoyed widespread populary because it is said to have the same analgesic otency as codeine without addiction potential nd with significantly lower incidence of underable side effects. Recent clinical trials have uggested that this product is difficult to distinuish from placebo in analgesic potency.[9] This nformation is somewhat surprising considering ropoxyphene's great popularity in recent years. dministration of propoxyphene in dosages of 5 mg four times a day for several months does ot produce drug dependence, however larger oses, 600-825 mg, of the drug daily for eight veeks cause slight, but significant abstinence yndrome upon withdrawal and dosages up to .3 grams have been associated with significant ncidence of withdrawal symptoms. Propoxyphene 32 or 65 mg) is also available in compound vith 227 mg of aspirin, 162 mg of phenacetin nd 32.4 mg of caffeine (Darvon Compound, Daron Compound 65) and as 50 mg of propoxyphene apsylate in combination with 325 mg of aceaminophen (Darvocet-N).

Although propoxyphene has been classed as ion-addictive and does not come under the puriew of narcotics laws, dependence may occur with epeated administration of higher doses. In view f these considerations and the greater cost of his drug than that of aspirin and codeine as well s the lack of convincing evidence of superior nalgesic potency, there seems to be little to ecommend it for routine use. Propoxyphene or Darvon Compound-65 may be useful for patients vith moderate pain who are unable to tolerate odeine-aspirin combinations and Darvocet-N may e useful for patients who do not tolerate aspirin ery well.

Ethoheptazine (Zactane)

Ethoheptazine, a structural analog of meperidine has been the subject of relatively few suitably designed clinical trials. In the usual dosages, 75-150 mg, significant analgesia may not be observable. To enhance its analgesic efficacy, ethoheptazine has been combined with acetylsalicylic acid (Zactirin). Clinical trials have shown that tablets containing 150 mg of ethoheptazine and 600 mg of aspirin produce analgesia equivalent to that achieved with 600 mg of aspirin alone.[7] Like propoxyphene, ethoheptazine may be useful in providing analgesia in patients with rheumatoid arthritis and other connective tissue disorders or in those who are on anticoagulant therapy, have peptic ulcer or are allergic to aspirin.

Pentazocine (Talwin)

Pentazocine (Talwin), a benzomorphan derivative with opioid antagonist action, is a relatively new analgesic that has been widely used because it can be taken orally. It is said to be devoid of addiction potential and produces fewer side effects than other narcotics. Oral doses of 50 mg are about equivalent to 60 mg of codeine. Side effects have been reported to occur. These include: increases in blood pressure and heart rate, sweating, dizziness, light headedness, nausea, and respiratory depression. Although the incidence of physical dependence is less with pentazocine than with other narcotics, reports of pentazocine dependence have been numerous. Among patients with chronic pain seen at the University of Washington Pain Clinic, the incidence of pentazocine addiction is low, but self-administration of doses up to 3000 mg per day has been observed. Despite those potential shortcomings, pentazocine constitutes an important addition in the pharmacologic armamentarium for pain relief. *This drug should be used with caution in patients who have had potent opiate narcotic analgesics administered and acting during the time of an intended course of Talwin therapy.*

Potent Narcotic Agents with High Addiction Potential

Morphine and Related Compounds

The beneficial actions of morphine in the treatment of refractory, intense pain are well known. Significant disadvantages and undesirable side effects complicate the management of pain with this drug and related agents. Many of the actions of morphine on the central nervous system can be classified as adverse. Unwanted sedation, mental clouding, inability to concentrate, lethargy, and generally, impairment of mental and physical performance may occur. These may or may not be desirable concomitants of analgesia with this drug, depending on the setting as well as the reasons for which the drug is used. In a chronic pain patient who could otherwise maintain a normal life-style, impairment of mental and physical performance is an undesirable action. In terms of the fearful, apprehensive patient who is about to have a surgery, general impairment of mental and physical performance may be a useful adjunct to pre-anesthetic medication.

Affective changes produced by morphine are not always perceived as pleasant; some patients experience untoward reactions such as anxiety, fear, or dysphoria. Nausea and vomiting frequently occur. Dizziness, respiratory depression and constipation are among the most common adverse effects. The development of tolerance and physical dependence and the specter of uncomfortable withdrawal limit the utility of this agent for long-term management. For these and other reasons the search for more effective analgesic agents with fewer side effects has con-

TABLE 2

Potent, Highly Addictive Analgesic Drugs

Generic Name	Proprietary Name	Approximate Adult Dose (mg)	Duration of Action (hrs)	Abuse Liability
Morphine and its Congeners				
Morphine		10	4-5	Relatively high
Papaveretum	Pantopon, Omnopon	15	4-5	Relatively high
Hydromorphone, dihydromorphinone	Dilaudid	1.5	4-5	Similar to morphine
Oxymorphone	Numorphan	1-1.5	4-5	Similar to morphine
Metopon		3-3.5	4-5	Similar to morphine
Heroin		3	3-4	Similar to morphine
Nalorphine (antagonist)	Nalline	10-15 (Not used for analgesia)		None
Naloxone (antagonist)	Narcan	(No analgesic activity)		None
Synthetic Analgesics of the Morphinan Series				
Racemorphan	Dromoran	5	4-5	Similar to morphine
Levorphanol	Levo-Dromoran, Levorphan	2-3	4-5	Similar to morphine
Dextromethorphan	Many cough mixtures	(No analgesic activity)		None
Levallorphan (antagonist)	Lorfan	(Very little analgesic activity at any dose)		None
Synthetic Analgesics of the Benzomorphan Series				
Phenazocine	Prinadol	2-4	4-5	Similar to morphine
Pentazocine	Talwin	45-60	2-3	Substantially less than morphine
Cyclazocine	Not available	0.3	4-5	None
Synthetic Analgesics of the Phenylpiperidine (Meperidine) Series				
Meperidine, pethidine	Demerol	50-100	2-4	Similar to morphine
Anileridine	Leritine, Apodol	25-35	2-3	Similar to morphine
Piminodine	Alvodine	7.5-10	2-4	Similar to morphine
Alphaprodine	Nisentil	50	Very short	Similar to morphine
Synthetic Analgesics of the Diphenylpropylamine (Methadone) Series				
Methadone	Dolophine	10	4-5, single dose; longer in tolerant indivs.	Similar to morphine
Dipiparione	Pipadone	20-25	4-5	Similar to morphine
Dextromoramide	Palfium, Dimorlin	6	4-5	Similar to morphine
Fentanyl	Sublimaze	0.2	4-5	Similar to morphine
Phenothiazines				
Methotrimeprazine (formerly levomepromazine)	Levoprome	15-20	4-5	None

inued, developing a varied group of strong analgesic drugs (Table 2).

The differences between morphine and its semisynthetic and synthetic-related agents have been over-estimated. The recent crisis produced by increased heroin abuse tends to reinforce the unbased belief that one opioid is more analgesic or euphorigenic or both than another. In equianalgesic doses most of the agents in Table 2 produce approximately the same incidence or degree of unwanted side effects, including euphoria. However, some patients may exhibit side effects with one drug and no side effects or different side effects with another. For these reasons, morphine surrogates are useful and welcome additions to the fight against pain. Pain that does not respond to oral administration of codeine with or without aspirin should be evaluated for a possible treatment wth opioid drug. The management of severe, intractable pain because of inoperable or recurrent cancer, becomes an exacting exercise involving a succession of therapeutic agents to maintain the patient in comfort. Physical dependence and tolerance occur whenever a narcotic is given in therapeutic dosages under these conditions, but in patients with a painful terminal illness, concern about addiction should be set aside in favor of fulfilling the primary obligation to ease the pain. One must be conservative however, keeping the amount of opiate analgesic drug as low as is consistent with pain relief. Narcotics should be reserved until non-narcotic drugs, other drugs, and other types of therapy no longer provide adequate relief.

Management of Narcotic Dependence With Methadone

In addition to its efficacy as an oral analgesic in managing chronic pain, methadone provides unique benefits in addicted patients in whom a narcotic is to be withdrawn.. Methadone is provided orally in a dosage sufficient to prevent withdrawal symptoms. The patient is observed and if significant withdrawal symptoms appear four hours later, an additional dose of 15 to 20 mg is given orally. More methadone may be given to suppress additional symptoms or if withdrawal symptoms reappear.

Once the patient has been free of withdrawal symptoms for 24 to 36 hours, programmed detoxification can begin. The stabilization dose can easily be calculated by totaling the number of milligrams of methadone required over a 24-hour period to keep the patient free of withdrawal symptoms. This amount is given as a single oral dose. One can approximate the amount of the stabilization dose from the patient's medical record. Usually 1 mg of methadone can be substituted for 4 mg of morphine, 2 mg of heroin, or 20 mg of meperidine.

In patients who remain free of withdrawal symptoms for a 24-hour period on a stabilization dose of methadone, 20 percent of the daily dose can be omitted each succeeding day until the patient receives no more. Should the patient have adverse responses to such a rapid reduction of dosage, a lesser decrement may be chosen. Although the patient may develop rhinorrhea and mild withdrawal symptoms, this method avoids completely the usual agitated withdrawal and allows safe detoxification of even the most severely ill patient.

Narcotic addicts in whom the narcotic is not to be withdrawn can be maintained free of withdrawal symptoms by maintenance doses of methadone. Although methadone maintenance is still experimental in the United States, its efficacy has been established and its benefits clearly outweigh its hazards. However, it should be emphasized that the maximum benefit of this kind of therapy can be obtained only in a setting in which adequate psychiatric, social and vocational programs provide a sound therapeutic milieu. The use of methadone maintenance in a narcotic addict is fraught with philosophic as well as legal problems if the physician does not have adequate time to provide the other necessary components of an adequate program.

Other Drugs

In addition to analgesic drugs, sedative-hypnotic, anti-anxiety, anti-depressant and tranquilizer medications may be of use. The blockade of depression and anxiety can alter patients' interpretation of painful stimuli as well as producing alterations in pain behavior. Sedative-hypnotic and anti-anxiety agents are associated with the development of tolerance and physical dependence. Chronic use and addiction to these agents may increase pain behavior in a given situation. Frequently detoxification from sedative-hypnotic and anti-anxiety drugs is required to improve the patient's affect and provide better control of pain. A list of drugs and appropriate relative potencies for substitution, stabilization, and withdrawal using phenobarbital as a long-acting agent during detoxification is found in Table 3. One must be cautious in estimating the tolerance of the patient and providing enough substituted phenobarbital to prevent agitation, and the occasional fatal seizure.

TABLE 3
Equivalent Dosages of Some Sedative-Hypnotic Drugs and Phenobarbital

Generic Name	Doses P.O.
Secobarbital	100 mg
Pentobarbital	100 mg
Diazepam	10 mg
Chlordiazepoxide	25 mg
Meprobamate	400 mg
Most barbiturates	100 mg
Glutethimide	500 mg
Whiskey	3-4 oz
Phenobarbital	30 mg

The method of estimating tolerance is simply to provide 200 mg pentobarbital orally, repeated at two hour intervals until the patient shows nystagmus, slurred speech, or sleep. Using the estimated relative potency (Table 3), one gives phenobarbital at 30 mg p.o./day per 100 mg of pentobarbital used to produce sleep. The total dose of phenobarbital so calculated may be given in divided doses over a day. Until tolerance to 300-500 mg of pentobarbital is determined, the danger of seizure activity and the relative necessity for substitution therapy is reasonably low.

Non-barbiturate Sedative and Anti-Anxiety Agents

Frequently patients undergoing detoxification procedures require sedation and anti-anxiety medication. Diphenhydramine (Benadryl), hydroxyzine (Vistaril) may be used to provide sedation and even sleep. Fifty mg every four hours will decrease the patient's anxiety and improve his tolerance to the withdrawal procedures, 100 mg i.m. or p.o. may induce sleep. These drugs are especially useful during detoxification from sedative-hypnotics where barbiturates or substances which have cross-tolerance to barbiturates cannot be used without complicating detoxification procedures.

Summary

Most patients with mild pain can be made comfortable with plain aspirin. Special aspirin preparations or other proprietary mixtures are little better than aspirin and are more costly. Their use should be reserved for patients who cannot tolerate aspirin.

Patients with moderate pain who do not respond to the nonaddictive analgesics usually derive sufficient benefit from aspirin compounded with small amounts of codeine or an agent of similar potency. The newer low-addiction-potential analgesics are more expensive and not demonstrably superior to codeine and therefore should be reserved for patients who tolerate codeine poorly.

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All pain's one malady with many names—Antiphanes [*408?-334? B.C.*]

The Office Management of Chronic Pain

Learning Factors

WILBERT E. FORDYCE, PH.D.*

Learning factors can play a role in chronic pain management in many ways, and the author describes these in detail.

WE CHARACTERISTICALLY LOOK at pain from the perspective of a disease model. Pain is considered to be a response to the stimulus of underlying pathology. That model is helpful and we do not propose here that it be discarded; however, when we are concerned with chronic pain a critical new element is added to the picture; learning or conditioning. This paper considers some of the ways in which learning factors play a role in chronic pain and the clinical implications.

Many patients with longstanding problems have more pain than necessary. This unfortunate state of affairs can occur because of the automatic effects of learning or conditioning. The striking reduction in the severity of a pain problem when nothing more than learning (or "unlearning") methods have been applied in treatment demonstrates the point.

Learning factors can play a role in chronic pain in several ways. One is how important people around the patient respond to the pain. The patient's physician, and other health care professionals, and the patient's family, for example, may come systematically to react to indications of pain in such a fashion as to promote and strengthen a pain habit. When that happens, the severity of the pain and the related functional impairment may be increased without any change in the underlying pathologic state. Commonly the original pathologic state may be effectively treated and thereby either diminished or eliminated, but the pain responses or behavior of the patient continue because they have come under the control of learning or conditioning factors.

A second way learning may play a role in chronic pain relates to the steps the patient himself takes to protect himself from the discomfort of his pain. When we have a pain problem we tend to develop certain actions which are designed to help us avoid experiencing the pain. For example, someone with a sore knee may limp. The limp serves the logical and useful purpose of minimizing pain. However if protective behavior is necessary for a considerable period the system becomes conditioned to them. We then may continue protective behavior without determining the extent to which the original reason we needed to protect ourselves is still present and active. These protective, or in the jargon of learning technology, "avoidance behaviors," are some of the most difficult to change or get rid of once they are established. Many patients develop a set of avoidance behaviors which may effectively serve to disguise from them that the original pain source is now gone or diminished.

Many people are puzzled and skeptical about the idea that learning or conditioning could cause a person to continue to experience pain with no current defect to produce the pain. The puzzlement in a large degree stems from a common misunderstanding about learning. We tend to think of learning as something we decide to do; something that we can turn on or off. In fact it does not work that way. About the best we can do is to help ourselves get into situations in which learning is likely to occur. If the conditions for learning are favorable, we will learn whether we want to or not. Our efforts at voluntary control are likely to have only a modest effect. An illustration of this point is the youngster who finds himself forced to scurry by the local cemetery at midnight during a thunder and lightning storm and who subsequently displays marked fear of the dark. That fear of the dark

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may persist for many years no matter how hard he tries to get rid of it. His system has been conditioned by a single event or a series of events and he is not able to influence the effects of that conditioning unless he enters into a systematic learning process designed to bring about change.

In recent years as we have come to recognize the potent effect of learning or conditioning on such body processes as pain, it has become possible to set up treatment programs based on learning principles designed to help a person get rid of his "learned" pain.

When pain medication is prescribed on a take only when needed (PRN) basis, the physician has set up an arrangement which actually may promote rather than discourage addiction and habituation. The "prn" regimen serves to let medication, and whatever beneficial effects it produces, become contingent upon or dependent upon hurting. As Skinner has pointed out in relation to the very extensive work which has been done on operant conditioning, letting the beneficial effect (positive reinforcer) become contingent upon a particular behavior is likely to have the effect of increasing the frequency or strength or persistence of that behavior. When you place your patient on a "prn" regimen you may be exposing him to a conditioning process which will increase the chances he will continue to ask for medication.

Physicians often prescribe bed rest as a part of the treatment for pain. If a patient is instructed to stop an activity when the pain becomes pronounced, an arrangement has been set up in which rest is contingent upon hurting. That is, if he hurts he gets rest. If he does not hurt he does not get rest. If rest is a beneficial effect or positive reinforcer for that patient, this working-to-tolerance regimen may serve to increase the chances he will hurt.

Every practicing physician has observed patients whose primary problem is a desire to gain his doctor's attention. The patient may be lonely, or depressed, or hypochondriacal. Whatever the case, he behaves toward his doctor in ways calculated to seize and hold his doctor's attention. Analyzed in learning theory terms, one might say that physician attention is a positive reinforcer which, when made contingent upon the expression of pain (or some other complaint), serves to increase the chances those complaints will persist.

A substantial amount of learned pain may be a result of the physician's efforts which were inadvertently productive of learning or conditioning; more often the action of others around the patient served to establish and promote a learned pain pattern. Family members protect the patient with pain by stepping in to take over difficult tasks. In doing so they may risk systematically providing the patient with "time-out" from unpleasant tasks each time he signals the presence of pain. Concomitantly, each time the patient tries physically demanding tasks, which previously have exacerbated his pain, he may be discouraged from making the attempt. Attempts at activity or well behavior may be punished or non-reinforced, whereas pain behaviors may be systematically reinforced.

There are other ways in which learning factors can have an effect. We are all familiar with the concept of secondary gain. Illness buys "time out" from anxiety producing, self-esteem threatening, or physically demanding situations. The "time out" because it is so much more pleasant than what would have happened had the patient continued into the noxious situation, serves as a potent reinforcer which may then increase the chances pain signals will continue to be displayed in order to gain the protection from the challenging or difficult situations.

Therapeutic Implications

If we can learn something, we can unlearn it. In selected patients, it becomes possible to set up a learning or conditioning program designed to reduce learned pain. The operant conditioning program for chronic pain has been underway for several years in the Department of Rehabilitation Medicine at the University of Washington School of Medicine. It is a multi-disciplinary program. The screening for patient selection involves a range of physicians: physiatry, family medicine, orthopedic surgery, psychiatry, neurosurgery, anesthesiology as well as psychologists and social workers. The program consists usually of five to six weeks of inpatient care and an additional one to two weeks of outpatient treatment, plus a diminishing frequency of follow-up contacts. The patient is admitted with a physiatrist as his attending physician. The program is carried out by a team including nursing personnel, a psychologist, social worker, rehabilitation counselor, a physical therapist, and an occupational therapist. Other health related professions are involved as necessary.

Description of the treatment may be found in the references[2-8] cited in the appended bibliography. The major dimensions of operant-based treatment for chronic pain are the concomitant focus on the reduction of pain behavior and the development and increase of effective well behavior. It is easier to reduce the severity of pain than it is to increase and establish firmly an effective repertoire of well behavior which will serve to keep the patient going after he leaves the intensive treatment environment. There are difficult and critically important issues relating to the necessity of replacing sick behavior with effective well behavior.

The operant program seeks to reduce medication intake, to reduce functional impairment from chronic pain, to reduce the rate and intensity of signals to the immediate environment that help is needed, and correspondingly, to increase activity level or movement.

Once current medication needs have been determined, the patient is put on a fixed time schedule of medications. That schedule is always at shorter intervals than he has demonstrated in initial observations. Medications are delivered in a simple color and taste masking vehicle, 10cc per dose, which has come to be known as the "pain cocktail." Dosage levels are gradually diminished and when the patient reaches the vehicle only he is so informed. All of this and every other feature of the program is explained to the patient prior to his admission.

The "pain behavior" of being immobilized or having to stop activity because of pain are managed primarily by shifting the patient from a working-to-tolerance to a working-to-quota mode. Tolerance limits for a series of pain relevant exercises are identified by direct observation. The patient then is assigned quotas which initially are less than his demonstrated tolerance limits for each exercise. These quotas are then systematically increased independently of how the patient feels. If the baseline observations have been carefully done and the initial quotas are set at modest levels nearly every patient will be able to work past his initial tolerance. Eventually exercise levels are limited at some desirable amount.

Attention to pain and well behavior is also treated in a systematic fashion. All of the treatment team maintain a neutral or socially nonresponsive style whenever the patient signals pain or weakness or distress. When, however, the patient is engaged in effective "well behavior," as when he is doing an exercise or interacting with others without signaling pain, they try to be as appropriately socially responsive as they can be. At the same time the family undergoes training to do the same thing. They too systematically rehearse "tuning out" pain behaviors and being socially responsive to effective well behavior. Again, all of this is spelled out to the patient, as well as to his family prior to the start of the program. In addition to programming attention from health care professionals and from family, patients keep records of their performance and post performance graphs on the wall. These graphs serve as signals to themselves, to visitors, and to staff that activity level is going up. Those around the patient are then in a position to be responsive and appropriately praising of these increments in performance.

Once the medication levels are down and activity level is up to a reasonable point, the patient begins to be assigned to a broader range of activities in which he can rehearse his newly restored functional capacities in a variety of settings. He may be assigned to a job in the hospital. He will become engaged in hospital recreational activities, and so on.

Usually after about five weeks of treatment, the patient then moves out of the hospital. If he is within commuting distance, he stays at home. If his home is remote, he lives in a nearby hotel or boarding house and commutes daily to the hospital. Whatever the case, he comes in every day and spends nearly a full day in the varied tasks making up his physical therapy, occupational therapy, job station, etc.

Those steps constitute the major efforts at the reduction of pain behaviors and the increase in activity level. Parallel with those efforts, depending on the needs of the individual patient, other elements of the treatment team, such as the psychologist, may be working with the patient and his family to help untangle some of the problems which may have made being well aversive or relatively unreinforcing. Sometimes these other problems amount primarily to some gaps in the patient's social skills. When that is the case, appropriate assistance may be provided.

From the foregoing review of the operant program for chronic pain, a number of implications for office practice, may be summarized:

1. In diagnosing problems of chronic pain, the physician should keep in mind that signals of pain from a patient are subject not only to influence by organic factors, but also by learning factors. There is no reason why the pain signals look different according to which of these sets of factors are operative at the moment. The physician should consider a learning-based explanation for the pain problem as a potential alternative to an organic-based diagnosis.
2. Prescription of pain medication should take into account the hazards of conditioning or habituation. The easiest safeguard is to let medications become time contingent rather than pain contingent. It is important to establish by observation what the current medication needs are. When that is known shift to a time contingent regimen which is at or above his current needs and is delivered *within* the time interval he requires. Dosage levels then can gradually be reduced (*e.g.*, over six to seven weeks).
3. Where rest or "time out" may have beneficial effects for the patient in relationship to circumstances in his life, or where the pain problem has persisted for a long time, the prescription of exercise in a working-to-tolerance mode may be contraindicated. Setting modest quotas and letting rest be contingent on work rather than pain may be helpful. Here again, establish current exercise tolerance limits and then set *lower* quotas to be gradually increased.
4. In recognition of the potency of attention from physicians and from family members, it is well to explore with the family in some detail what actions they take when the patient is engaging in pain behavior and well behavior. Efforts to modify the pain problem and the related functional impairment may be inadvertently sabotaged or upset by ill-advised family responses. They may need to be reprogrammed.
5. Chronic pain patients often represent a failure of health care system to solve a problem. He—the patient—is trapped because you may, in effect be "the only game in town". It is understandable that he is often suspicious, perhaps surly. The chances are good he has been told (or it has been hinted at) his pain is imaginary or psychogenic. He might be angry and have a chip on his shoulder. Your task and your communication with him, may be facilitated by respecting his anger and the reasons for it.
6. The frustrating problems of chronic pain which have failed to be helped by a multiplicity of treatment approaches, may be helped by referral to an intensive treatment center providing sophisticated and well integrated learning-based treatment.

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He is currently serving as President of the Minnesota State Board of Medical Examiners and as President-Elect of the National organization, which includes state medical boards from the fifty states and the District of Columbia.

Doctor Horns was actively involved in the development of the Flex examination for licensing physicians which has been accepted by nearly all of the fifty states as well as the District of Columbia and the Province of Saskatchewan, Canada.

There is no real evil in life except great pain; all the others are in the imagination and depend on the way one thinks of things. All other evils find their remedy either in time, or in moderation, or in strength of mind; reflection, devotion, philosophy can soften them.—Marie, Marquise de Sévigné (1626-1696)

The Management of Pain with Nerve Blocks

RICHARD G. BLACK, M.D., BA Sc (EE)*

SOME 90 YEARS AGO, Carl Koller pioneered the clinical use of regional anesthesia by surface application or local infiltration of cocaine.[1] In 1884 Halsted injected cocaine into a nerve trunk, thus obtaining the first conduction anesthesia.[2] During the next five decades, regional anesthesia was widely used by surgeons because of its great advantages over general anesthesia and analgesia as then administered. Advances in the safety and comfort of general anesthesia resulted in a corresponding decline in regional anesthesia. Now scientific understanding has resulted in its increased use in surgical and obstetrical anesthesia, and as a powerful diagnostic, prognostic and therapeutic tool in the treatment of painful conditions.

Basis for Use

Controlled interruption of specific sensory, somatomotor, and autonomic pathways is the basis for the utilization of nerve blocks as diagnostic, prognostic, and therapeutic tools in the management of pain states. Sensory block by interruption of the afferent limb relieves pain, interrupts abnormal reflex mechanisms and isolates abnormal peripheral foci of noxious stimulation. Somatomotor block relieves skeletal muscle spasm. Sympathetic block eliminates vaso-motor and sudomotor disturbances and abnormal sensory input mediated through visceral afferent fibers accompanying the sympathetic fibers.

Interruption of one or more of these pathways often results in pain relief. The pain free state produced is often sustained by poorly understood phenomena prolonging beneficial effects by hours, days, sometimes weeks or more beyond the return of nerve conduction. Whether this is due to the interruption of activity of self-sustained neuronal pools in the neuroaxis or else desolution of a peripheral "vicious circle" based on strong segmental sensory input and maintained muscle spasm or vasospasm is unknown.

Fundamentals for Use

Nerve blocks must not be undertaken casually. The physician who plans to inject a toxic agent into a patient and uses the results obtained to make a statement affecting the patient's diagnosis and therapy must be fully cognizant of all the possible consequences. He should have a working knowledge of the anatomy involved, the pharmacology of the agents used, the clinical results usually obtained and the possible side effects or complications to be expected and a plan for their management. The practitioner—no matter what his specialty or background—must act as a physician with the responsibilities and obligations this entails, rather than as a technician with an expertise in inserting needles. A detailed history and physical examination not only makes the physician familiar with the problem at hand but affords an opportunity to establish rapport with his patient.

The physician must consider whether nerve blocks are indicated in this particular case. Poor or routine selection of patients for analgesic blocks leads to unsatisfactory results. If nerve blocks are indicated, an overall plan of action should be established. It is necessary to select the best technique, the optimal site of injection, the most suitable drugs to be used and what controls are to be applied to the situation. Thorough knowledge of pain syndromes, expertise with the technique of various blocks and familiarity with the pharmacology and toxicology of the drugs used are required.

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See editorial, page 223.

The patient should be clearly informed about the various phases of the procedure, the purpose of the block, the anticipated effect, and the plan for the future. The patient's cooperation is essential and an informed patient is more likely to be a cooperative patient. Depressant drugs and analgesics are contraindicated when blocks are being used for diagnostic or prognostic purposes. A drugged patient cannot report his subjective responses clearly. If a patient cannot be controlled with the spoken word, an ultra short-acting intravenous barbiturate is sometimes helpful.

Anatomical knowledge necessary for skill in performing nerve blocks consists of thorough familiarity with pain sensitive structures and their peripheral and segmental innervation. The course and branches of peripheral nerves, their points of access and fascial planes in which they lie should also be well known. Localization of the desired nerve can be accomplished by gently eliciting an appropriate paresthesia, confirming the position of the needle by Xray with or without prior injection of contrast media, observing the effects of small quantities of anesthetic solution, and by using low levels of electric current for stimulation. Alterations in muscle activity and sensory responses should be appropriate to the distribution of the nerve being approached since significant but functionally meaningless responses may often be obtained from nearby periostium or other sensitive structures.

It is important that the physiological effect, dosage and toxicity of any medication administered to a paitent be known by the physician. This no less true for the anesthetic drugs and their additives that are injected for nerve blocks. Systemic reactions occurring when an injected drug is absorbed indicate either a high blood level of the drug or a true allergy to it. Since the most common error is overdose of the drug it is especially important to know the milligram per kiligram dose limits for each of the drugs used and to understand the dynamic relations between rate of absorption, blood level and the use of vasopressors. A good practice is to think of milligrams or micrograms of drug injected rather than volume of solution injected. The physician should also be cognizant of the side effects of injected drugs. The feeling of impending doom, tachycardia, excitement, verbosity or incoherent speech produced by the absorbed adrenalin which was added to the injection primarily as a vasoconstrictor, should not be mistaken for the central excitability sometime accompanying an overdose of local anestheti agent. The expected duration of the analgesi block and the fiber size affected are necessary fo interpreting the result of the block. Also usefu are the times when certain complications might b expected.

Analgesic nerve blocks may produce side effect or dangerous complications. It is necessary tha these be recognized and that it be known when i is safe to discharge a patient after a block. Complications may be short term occurring within on to ten minutes of the injection, as may follo inadvertent intravascular or subarachnoid injection or an acute allergic reaction. Longer term complications may be related to the increasin blood level of the anesthetic agent due to its absorption or to diffusion of the drug to a paradura site resulting in paralysis of a vital function. Thes details are as important for study as the technique of the blocks.[3]

No block—other than infiltration of two t three mls. of local anesthetic into superficial part of the body should be done without having equipment and personnel available for cardiac and respiratory resuscitation. For blocks near the neura axis or involving large quantities of anesthetic th patient should be "NPO" for eight hours. Unexpected complications due to a prior health problem need not occur if an adequate history an physical examination are done by the physicia performing the block.

A selection of needles should be available. I is important that these be sharp and free from burrs. Burrs may be readily produced by handling needles roughly or hitting bony landmarks to vigorously (Figure). These burrs result in tissue damage as the needle is withdrawn. Disposable needles of softer steel and with long fine tapers are more susceptable to formation of burrs and give the operator less feel for tissue planes than equally sharp but blunter reusable needles.

The Use of Nerve Blocks in Pain Problems

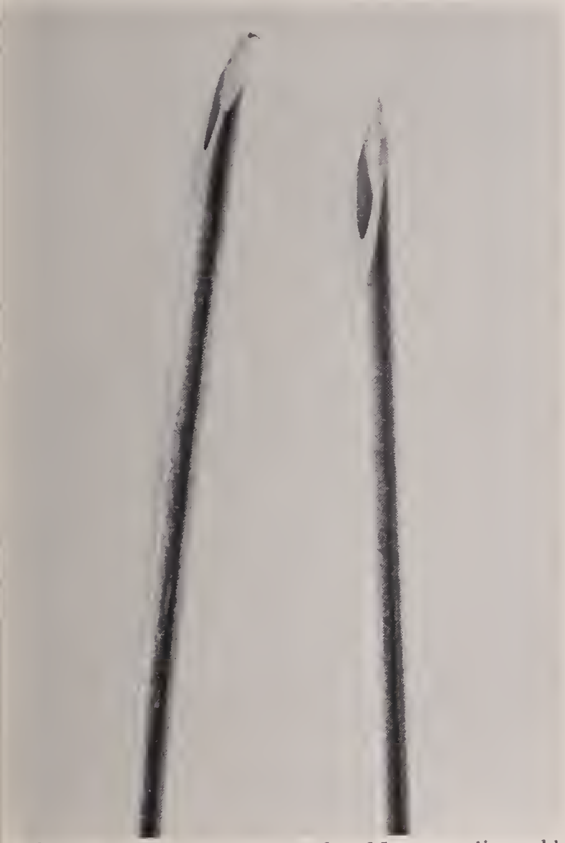
Local Infiltration

Local infiltration of a local anesthetic agent alone or in combination with a corticoid compound is a simple and effective method of managing many painful musculoskeletal disorders, a variety of myofascial syndromes with trigger mechnisms and scar neuromata. Most of these conitions are superficial and can be treated in the hysician's office, provided proper precautions are bserved with regard to total anesthetic dosage sed and that resuscitative equipment is available the case of an allergic reaction.

In managing the scar neuromata, no anesthetic gent should be injected until the most acutely ensitive area of the scar is localized with the ry needle tip. Then, two or three ml of local nesthetic agent should be injected forcibly. This ill momentarily be very uncomfortable for the atient but will produce a much better long term esult. Several injections are usually required for ermanent relief. The patient should be warned hat the area will be more painful for a short hile after the anesthetic has worn off but will e improved in a few days.

Sympathetic Block

Block of sympathetic pathways controls pain associated with reflex sympathetic dystrophy, peripheral vascular disease, thoracic and abdominal visceral disorders and certain musculoskeletal disorders. Interruption of these pathways can be achieved at any one of four sites: subarachnoid space, peridural space, paravertebral or prevertebral regions, or peripheral nerves. Segmental paravertebral or prevertebral injections are preferred for diagnostic, prognostic, and certain therapeutic blocks, because the block is more specific and in the case of prevertebral blocks only sympathetic nerves are likely to be involved.



Figure—Macro photograph of a 25 gauge disposable eedle damaged by impingement on bone. The burr so formed can do significant tissue damage as the needle is withdrawn. The long taper seen here is more susceptible to formation of burrs than a shorter taper and as well gives less feel of the tissues being traversed.

Studies with contrast media have demonstrated that injections into the proper fascial plane can result in a block of the entire peripheral sympathetic outflow. Needles need only be placed in any one of three critical sites.[4] Up to 12 ml. of solution injected into the proper fascial plane near the stellate ganglion spreads to involve the ipsilateral sympathetic chain from the middle cervical to the fifth thoracic ganglion, so that all the sympathetic fibers to the head, neck, and upper extremities and thorax are interrupted. This spread is assisted if the patient is upright and impeded if scarring secondary to tracheostomy or anterior fusion is present. Similarly solutions injected near the celiac plexus spread sufficiently to interrupt all sympathetic fibers to the abdomen, and injections through a needle with the tip at the anterolateral surface of the second lumbar vertebra interrupt all ipsilateral sympathetic pathways to the lower extremities and pelvis. At the same time the above sympathetic motor fibers are blocked, the visceral afferent fibers accompanying them are also interrupted. This is especially significant in the abdomen where spectacular relief of pain from widespread malignancy or chronic pancreatitis is often obtained. Infiltration of the brachial plexus around the axillary artery will result in sympathetic block of the forearm and hand.[4] Posterior angle intercostal blocks will result in segmental sympathetic block of the chest wall.

Cervicothoracic (Stellate Ganglion)

The easiest and most practical method of blocking the cervicothoracic nerves is by the anterior paratracheal technique.[5] With the patient raised to the sitting position, as tolerated shortly after the injection, 10 to 12 mls. of solution will diffuse sufficiently to produce a cervicothoracic sympathetic block. This is usually termed a stellate ganglion block. It is useful in differential diagnosis of head, neck and chest pain and as a prognostic procedure in chronic pain syndromes for which surgical or chemical sympathectomy is anticipated. In the treatment of reflex sympathetic dystrophies, stellate ganglion blocks may be carried out on an alternate day basis combined with daily physiotherapy.

Sympathetic blocks are of limited value in acute vasospastic disorders such as Raynaud's disease and are contraindicated during anticoagulant therapy because of the risk of hemorrhage. They are of limited value in predicting the effects of sympathectomy in chronic peripheral vascular disease.

Prevertebral Sympathetic

Prevertebral sympathetic blocks may be used in blocking the lumbar sympathetic ganglion. A single injection of 15 to 20 ml. of anesthetic agent at the L2 level is usually sufficient to produce a temporary sympathectomy of the ipsilateral lower extremity and low back. This block is often performed on ambulatory patients to assist in the management of long term intractable low back and extremity pain. While the vaso dilatation produced by this block can result in significant postural hypotension, it is generally well tolerated.

Splanchnic Nerve (Coeliac Plexus)

Since the splanchnic nerves contain all the sympathetic and visceral afferent pain fibers in the upper abdominal viscera, a block of these nerves is useful in managing acute and chronic pain due to disorders of these viscera. A coeliac plexus block with short acting local anesthetic aids in differential diagnosis of abdominal pain from body wall pain and is especially useful in predicting the ability of the patient to tolerate the cardiovascular effects of a chemical or surgical splanchnicectomy. If several anesthetic coeliac plexus blocks have shown consistent pain relief and no disabling cardiovascular effect, injection of 25 mls. of fifty percent alcohol into each of two bilaterally placed needles is effective in the management of abdominal pain in terminal disease. When distorted anatomy secondary to retroperitoneal and upper abdominal malagnancies is present, several attempts may be necessary before a satisfactory block is obtained.

Somatic Nerves

Somatic nerve blocks are primarily useful as an aid in diagnosis of pain by isolation of the nerve pathways involved, for treatment of acute musculoskeletal pain where reflex muscle spasm is present, and in the treatment of acute pain. Peripheral nerve block is helpful in managing the exacerbations of central pain otherwise controlled by medication.

Neuralgia is usually the symptomatic expression of a neuropathy, radiculopathy, or myelopathy caused by inflammatory, circulatory, toxic, degenerative, metabolic, or neoplastic disorders. Its cause must be carefully sought and if possible removed.

Cranial Nerve

Blocks of the various cranial nerves and their branches are useful in the diagnosis and management of severe head pain. Alcohol block of the Gasserian ganglion has been used in the past for the treatment of trigeminal neuralgia or cancer when neurosurgery is contraindicated. It should only be used when systemic medications fail and the more controllable thermocoagulation of the fifth nerve root is not available. Glossopharyngeal nerve block just below the jugular foramen aids in management of glossopharyngeal neuralgia as well as in the temporary control of pain in cancer of the throat.

While not a cranial nerve, the greater and lesser occipital nerves are easily blocked and should be considered as culprits early in the diagnosis of head and face pain.

Spinal Nerves

Paravertebral block of the upper cervical nerves that contribute to the cervical plexus can control severe pain in the suboccipital region of the neck and posterior portion of the head. Such pain often results from whiplash injury, but in older people may be due to arthritis, fibrositis, or myofascial syndromes. Paravertebral blocks or local infiltration of tender soft tissues is immediately beneficial and, when combined with physical therapy may effect prolonged relief.

Paravertebral block of the lower cervical nerves may be used to treat cervicobrachial neuralgia or other disorders of the shoulder girdle and upper extremity and to differentiate pain of peripheral origin from pain caused by disorders of the central nervous system.

Suprascapular block can control severe pain in the shoulder joint due to musculoskeletal disorders, such as bursitis or arthritis and the referred pain f suprascapular nerve entrapment. Treatment of xtremity and joint pain is most effective when combined with stellate ganglion block. Physiotherpy is a necessary supplement to block therapy if prolonged relief is to be obtained in these problems.

Pain having a radicular distribution may be managed by paravertebral block of thoracic or lumbar spinal nerves. This is useful in treatment of problems secondary to orthopedic disorders, infections, trauma, severe post operative pain, cancer pain and musculoskeletal pain of the trunk.

Intercostal blocks to relieve severe post operative thoracic and abdominal pain or pain due to fracture of ribs, sternum or cartilages result in improved ventilation and prevention of atelectasis and pneumonia. Three to five mls of 0.15 percent tetracaine or 0.50 percent bupivacaine solution with epinephrine (1:200,000) will relieve pain for six to ten hours or longer.

With few exceptions, segmental spinal nerves are mixed nerves. Therefore the sensory nerves cannot be blocked without affecting the motor nerves. Injection of alcohol here to produce prolonged interruption is contraindicated, because in addition to paresis or paralysis, somatic nerve blocks with alcohol are often followed by a chemical neuropathy with neuralgia, which is often more severe than the original pain. These blocks should only be considered when surgical rhizotomy is contraindicated and when the patient's life expectancy is less than three months.

In the hands of the experienced physician, segmental spinal epidural block may be used anywhere along the neuroaxis. Any number of segments can be blocked with this technique with only one injection and with proper supervision the effect can be extended for days using the continuous technique with an indwelling catheter. Segmental peridural block of the middle thoracic nerves is probably the most effective method of relieving severe pain of pancreatitis and biliary, renal, and ureteral colic. It will also control pain associated with multiple rib fractures, thoracic and abdominal surgery, amputation of extremities and reflex sympathetic dystrophy and relieves acute thoracic or lumbosacral neuralgia due to herniated intervertebral disk. The relief of muscle spasm obtained from this type of block greatly assists more definitive therapy such as traction and bed rest.

Single dose or continuous spinal subarachnoid block may be used. The graded isobaric diagnostic block in which gradually increasing concentrations of anesthetic solution, from 0 to sufficient levels to produce sympathetic blockade then sensory blockade and finally motor blockade or surgical anesthesia are useful in diagnosing the patient's reaction to his pain problem and gives some indication of the organic intensity of his pain. Subarachnoid block with alcohol or phenol produces a chemical posterior root rhizotomy, which is an effective substitute for neurosurgery in patients who are in poor physical condition or who refuse operation. This is particularly effective in the management of cancer pain, with relief found in our institution in slightly more than 50 percent of patients, fair relief in 30 percent and no relief in 20 percent. About one quarter of the patients exhibit complications in the form of bladder and bowl dysfunction and paralysis or weakness of the lower extremities. The duration of the pain relief obtained varied from several weeks to many months, with an average of about three months. Candidates for neurolytic blocks should be referred to a center where such procedures are being done regularly.

Conditions for Optimum Results

Optimum results with nerve blocks can only be obtained if these are undertaken in a systematic manner and adequate records kept. Detailed neurological examination of the involved area of the body must be done immediately prior to any block and repeated at the time the patient reports any subjective relief from pain. The exam should then be repeated at the height of the block, and, when the patient again reports the return of his symptomatology to evaluate the cutaneous sensory level and motor involvement related to pain relief. It is only by having the result of all these examinations available in a systematic form together with the patient's subjective report that an adequate diagnostic examination can be satisfactorily completed. The use of saline injections and anesthetic injections with different durations of action will help sort out the one third of patients who tend to be overly helpful in their anticipation of a good response.

Clinical records should include a consent form, an entry in the progress note section of the patient's chart in which the total plan of the diagnostic block procedure is outlined, a detailed block record and an entry in the clinical log book stating the procedure done and the personnel involved. Follow-up visits or phone calls are made at a time when all effects of the block have worn off. Patients are instructed to keep a diary of their observations, activity and medications during the course of the block.

The skillful use of nerve blocks has an important role in the management of chronic and acute pain problems. It is important that these be performed with responsibility, skill and understanding so as not to bring any harm and to give the earliest possible relief from pain.

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Reading List

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> The experiments of M. Delafontaine having again raised an outcry against the noble science, from the apparent absence of any benefit likely to arise from [mesmerism], beyond converting human beings into pincushions and galvanic dummies . . . Mrs. Johnson may shut up her laboratory for American Soothing Syrup; mesmerism is the only panacea for those morning and evening infantile ebullitions which affectionate mammas always assign to the teeth, the wind, or a pain in the stomach, and never to that possible cause, a pain in the temper. Mesmerism is "the real blessing" to mothers, and Elliotson the Mrs. Johnson of the day. We have tried it upon our Punchininny, and find it superior to our old practice of throwing him out of the window.*

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*"The Advantages of Animal Magnetism." **Punch**, 1841.

External Electrical Stimulation

As a Treatment of Chronic Pain

DON M. LONG, M.D., PH.D.*

Cutaneously applied electrical stimulation appears to be a feasible means of reatment for a significant percentage of patients incapacitated by chronic pain. The initial beneficial effects upon the pain appear to be maintained for at least one year and most kinds of chronic somatic pain respond at least in part to this form of therapy. Patients with central pain and severe peripheral neuropathies are rarely benefited. Patients with psychogenic pain have routinely been worsened or at best not helped on a long term basis by these stimulation procedures. While it is still premature to categorize the benefits of cutaneous electrical stimulation in pain treatment it does seem likely that this form of therapy will play an expanding role in the management of chronic pain.

In 1965 Melzack and Wall[3] published an article in which they postulated that a gate for pain existed in the posterior spinal horns and that modification of the perception of pain might be possible by blocking the gate with nonpainful stimuli.[3] The publication of this gate theory of pain reawakened clinical interest in the treatment of chronic pain and has opened several new avenues of therapy. The first techniques to arise from this theory utilized the implantation of stimulating devices around large peripheral nerves or over the posterior columns of the spinal cord to produce the pain blocking sensations.[4] It soon became apparent that most patients with pain were not candidates for these types of procedures as they currently exist. In an attempt to find a reliable test for ultimate success or failure of one of the types of implanted stimulating devices we investigated cutaneous application of electrical stimulalation for pain relief. Our initial efforts with commercially available crude stimulators were so encouraging that a concerted effort was begun to devise a more refined stimulator to evaluate and treat patients with chronic pain. The prototype of these stimulators was produced in 1971 and has now been in clinical trials for two years.[2] Several other commercial stimulators have been developed subsequently and at least two of these devices have received extensive clinical evaluation.[1] It is the purpose of this paper to describe the use of these external stimulators in the first 400 patients suffering from chronic intractable pain evaluated and treated at the University of Minnesota Hospitals Pain Center. Follow-up evaluations of almost one year are now available for comparison with the initial results.

Patient Evaluation and Treatment

All patients were admitted to the University of Minnesota Hospitals and underwent complete physical evaluation to ascertain the cause of the pain problem and to eliminate the possibility that definitive therapy might be more appropriate. No patient was included in the program until all reasonable therapy for the underlying disease was exhausted. All standard modes of pain relief had failed in these patients. All underwent complete psychiatric examination.

As the first step of pain relief, external electrical stimulation was employed. The stimulator was first applied to the area of pain by a nurse in charge of the program or by one of the physicians involved. No special set of parameters

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See editorial, page 225.

of stimulation were utilized and the location of stimulating electrodes as well as the parameters of stimulation were derived on a purely empiric basis. After the first or second stimulating session the patient was given complete control of the device and was able to move the electrodes and change the stimulation as seemed most appropriate. Two or three days hospitalization was usually required to study thoroughly the patient's response to the stimulator and to find optimum placement of electrodes and the best stimulus parameters for pain relief. Three or four sessions of approximately three hours each were usually chosen and then in the second or third days the patients were allowed to vary time and frequency of use. If stimulation appeared to be satisfactory for relief of pain, a personal stimulator was obtained and the patient discharged to continue the use of the device for one month. If stimulation did not bring about adequate pain relief, the evaluation proceeded along other lines.

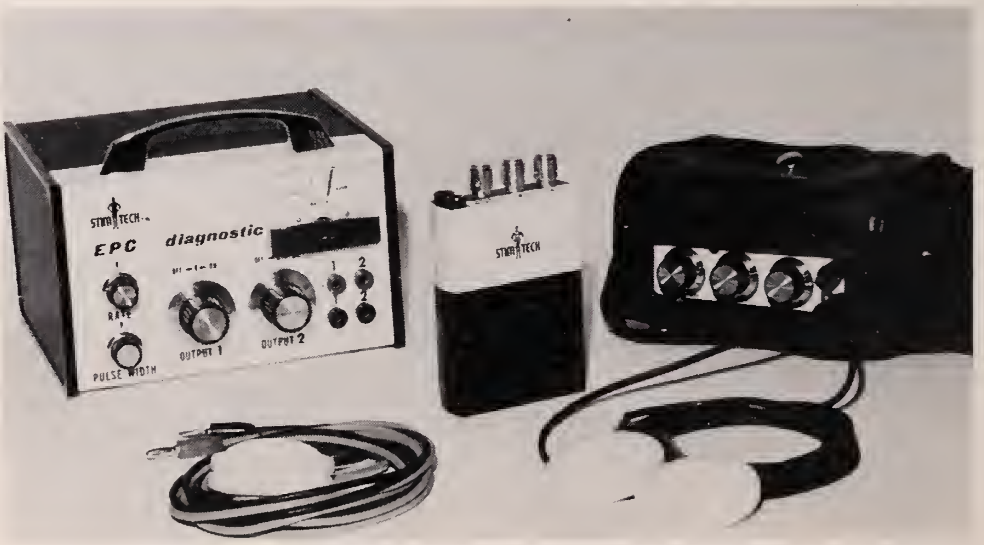
The Stimulators

Representative samples of the family of stimulators produced by Stimulation Technology* employed for most of this study are seen in the Figure. These stimulators produce a modified square wave pulse with variable voltage, frequency and pulse widths. Electrodes are stainless steel discs covered by sponges and electrical contact is made by moistening the sponges with water or an electrolyte fluid or paste.

A second family of stimulators has been produced by the Medtronics Corporation,† and several examples of these units have been used in this study as well. These stimulators produce a spike with variable voltage and frequency but without the ability to change pulse width. The patients to be reported have been evaluated with a model of these two families of stimulators.

Results

Four hundred patients were initially studied. There were 238 females and 162 males. The age span was 19 to 86 years. Two hundred and three patients were initially evaluated. Of these 150 underwent a randomized trial of stimulation. Fifty patients were stimulated in the standard manner described. Fifty patients had the electrodes attached and the unit apparently turned on but the electrodes were not energized. Fifty patients had the electrodes energized at subliminal levels. Following 24 hours of sham stimulation, actual stimulation was begun. There was so little placebo response in these patients that this random stimulation technique was abandoned after the first 150 patients. A program of evaluation of each patient according to the treatment protocol was then begun. Use of the stimulator, parameters of stimulations, and results were recorded in detail. Fifty-three patients during this period of time failed to complete this protocol so these first 203 patients are excluded from the numerical data to be reported. This includes all those utilized to ascertain placebo effect and those failing



Figure—The standard stimulator for hospital use is pictured on the left. The stimulator on the right is the original portable stimulator for home use. The miniature unit in the center is the latest model for personal use. All have the same electrical capabilities.

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†3055 Old Highway Eight, Minneapolis, Minnesota 55418.

o follow the protocol exactly.

Following these initial evaluations of the intrument and its use, 197 consecutive patients were treated by a single nurse experienced in he use of the stimulating device according to the protocol described. The disease states treated are listed in Table 1. These patients all were conidered failures of all conventional forms of therpy and represented the most difficult pain mangement problems. At the time of discharge from he hospital the following results were obtained with the use of external stimulation for pain conrol. Seventy-eight patients reported excellent relief of pain and were able to tolerate an increased activity level and the beginning of a decrease in pain medications. Fifty-four additional patients reported a beneficial effect upon the pain though pain relief was less adequate and in these patients it was problematical whether external stimulation alone would be adequate for long term therapy. There were 65 failures. Most of the failures occurred in two groups of patients. The first was a group of 20 patients specifically chosen for inclusion in the study because of overt psychiatric disturbance. None of these patients had a bonafide reason for pain and all were prejudged to have serious psychiatric disease. Eighteen of the twenty patients were immediate failures and of the two that initially described good results, one failed to maintain the beneficial effects of stimulation for more than two weeks and the other failed in one month. The second large group where failure became predictable was pain of central nervous system origin such as the thalamic syndrome, spinal cord injury, and the pain of serious peripheral neuropathies. The majority of patients left the hospital with a stimulating device for a one month minimum home trial though obviously many were not expected to find the use of external stimulation satisfactory control for their pain.

Late Followup

Almost one year later these patients were surveyed by mail questionnaire and by telephone. One hundred and four patients, 64 males and 40 females responded with a complete usable questionnaire. The diagnoses and results in those patients using the device for one year are found in Table 2. The majority were suffering from chronic low-back pain with chronic adhesive arachnoiditis. Seventy-one of all patients were able to maintain satisfactory pain relief. This was reported by the patient to be excellent in ten, good in 33 and fair in 32. However, when the patients categorized their relief it was considered satisfactory only if their pain was under better control than with any other previous form of therapy, and if they were satisfied enough to continue using the device. Four patients reported fair relief of pain without feeling their pain control was really satisfactory. Fifteen patients had some effect upon pain without adequate relief in their opinion. Only 14 patients were unable to obtain relief of pain. These 29 of the 104 patients felt that their pain relief had been inadequate and that they would not buy a stimulating unit again. The remainder, however, indicated that they would purchase or rent a stimulator if given a second opportunity to decide. Sixty-six of the

TABLE 1

Results of Afferent Stimulation at Time of Initial Hospital Discharge

	Results	
	Beneficial	No Benefit
Chronic low-back pain with verified arachnoiditis	73	16
Stump and phantom limb pain	5	1
Psychogenic pain	2	18
Cancer	3	2
Chronic low back syndrome secondary to lumbar osteoarthritis	10	0
Chronic cervical syndrome secondary to cervical osteoarthritis	10	0
Central pain states	2	2
Peripheral neuropathy	1	6
Post herpetic neuralgia	3	1
Others	23	19
TOTALS	132	65

TABLE 2

Diagnosis		Results	
		Success	Failure
Chronic low back syndrome with verified arachnoiditis and/or lumbar osteoarthritis	82	61	21
Chronic cervical syndrome secondary to cervical osteoarthritis	6	4	2
Post herpetic neuralgia	3	2	1
Thalamic syndrome	1	0	1
Headache (migraine 3, chronic tension 2)	5	3	2
Carpal tunnel syndrome (postoperative)	1	1	0
Chronic prostatitis	1	0	1
Brachial plexus injury	2	2	0
Chronic pancreatitis	1	1	0
Phantom limb pain	1	1	0
Multiple abdominal operations	1	0	1

patients were able to markedly reduce or virtually eliminate the use of pain medications and 48 reported significant increases in activity levels. The average length of use of the stimulator was nine months. The average patient used the stimulator for ten hours per day and received 3.5 hours of relief after discontinuation of the stimulator.

Inspite of the fact that the majority of the patients treated with this form of therapy were happy with the pain control they achieved, there were numerous objections to the methods. The majority relate to the design aspects of the stimulator and not to the quality of pain control. Patients requested a smaller, less cumbersome unit and improved electrodes with better means of applying electrodes on a semipermanent basis. A frequent complication was skin irritation following prolonged use of the device. This responded to the application of cortisone cream in most instances, but especially in patients that had undergone previous radiation therapy, was occasionally severe enough to stop the treatment. Unfortunately, several patients with the best results in terms of pain relief suffered from the most serious skin problems and the quality of their relief was seriously compromised by the skin irritation.

It is of interest to note that 82 of the patients wanted additional therapy for pain and this figure almost uniformly represents a desire to be rid of the necessity of using the stimulator for pain relief. These patients represented failures of all conventional forms of therapy and subsequent to external stimulation the only feasible form of treatment of the pain appeared to be implantation of a spinal cord or nerve stimulating device. When confronted with the possibility of a major operation and after considering the possible hazards of implantation of a peripheral nerve or posterior column stimulator only four patients wished to go ahead with treatment of this kind. The remainder preferred to continue using the external stimulator in the hopes that improved instrumentation would ease the technical problems of stimulation.

Discussion

These results are encouraging considering the fact that this is simple form of treatment applied to a group of the most difficult management problems in the area of chronic pain. More than 30% of these patients could be managed satisfactorily using external stimulation alone and followup of continued evaluation of almost one year's duration indicates that these good results are maintained. The major problem precluding the use of the device or limiting its effectiveness has been chronic skin irritation and the lack of an easily applied electrode. The principle of pain treatment by this method appears well established by these data and it should be possible to make these stimulating devices much more effective by improved engineering design. The difficulties with chronic skin irritation are a much greater problem and must be solved if these devices are to attain their maximum use in the treatment of chronic pain.

A brief, almost anecdotal experience with acute pains of less severity such as the acute cervical and low-back syndrome, a variety of sprains, ligamentous injuries and tension headaches suggest that this form of therapy may be of even greater value in these less serious problems. This remains to be investigated in a systematic way.

Probably the most important factor in dealing with patients using these stimulators for chronic pain relief is the availability of consultation for patients with problems in respect to the use of the device and engineering consultation for repair and modification. We have attempted to solve this time consuming necessity for ongoing consultation by several mechanisms. The use of the device is primarily managed by a nurse well trained in dealing with pain patients and skilled in the use and theory of the instrument. A clinic has been established where these patients can come both for initial evaluation and instruction in the use of external electrical stimulation and for continued help with the resolution of their long term management. It is not necessary for a physician to be involved in this phase of the patients care except on a consultative basis and the majority of the difficulties can be solved by a combination of expert nursing care and the availability of technical assistance with the stimulator.

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Facets in Back and Sciatic Pain

A New Approach to a Major Pain Syndrome

C. NORMAN SHEALY, M.D.*

Majority of back and sciatic pain syndromes appear to be the result of mechanical alterations in the small facet joints. Seventy percent of 275 patients seen by author had pain related primarily to facet distress.

ALMOST 25% OF AMERICANS sustain injuries to the back or spine within their life-times and approximately *10% of all* Americans have some *permanent impairment of the spine.*[1] Beals and Hickman[1] reported that only 38% of patients with compensation-related back injuries returned to work within six months of onset, and at least 31% remained unemployed for over two years. Some reports are even more pessimistic, especially when surgery is performed. The return to work is dependent upon both psychologic and physical factors.

Once the patient has had a surgical procedure, the chances for return to work are even slimmer. Each additional surgical procedure and each month of additional inactivity further reduce the chance of return to employment.

The cost of back injuries to the function of society is inestimable, but must be in the realm of billions of dollars annually in terms of non-productivity, compensation payments, and medical costs. For instance, in Wisconsin each year it is estimated that 75% of compensation payments are paid to back injured patients who represent only 3% of the total compensation claims.[2] Medical expenses, once an individual has surgery, mount rapidly. One 32-year-old woman recently reported medical-surgical-hospital costs of $160,000 over the previous eight years.

Considering the fact that 30-40% of patients undergoing a "laminectomy" for a presumed ruptured disc fail to achieve pain relief, great care should be exercised in a decision for surgical intervention.

Prior to 1934 it was generally recognized that much back and sciatic pain resulted from disorders of either the spinal facets or of the sacro-iliac joints. Following Mixter and Barr's[3] description of the "ruptured disc" most neurosurgeons and orthopedists became convinced that back and sciatic pain must be due either to a ruptured disc or to psychosomatic disorders. Despite the widespread use of myelography as a diagnostic aid, at least one-third of active neurosurgeons operated purely on "clinical" grounds. Even myelography has a 30% "false positive" risk;[4] furthermore, it seems likely that Pantopaque® is the major inciting cause of the often devastating cases of arachnoiditis complicating disc surgeries. It seems essential that patients be subjected to risky diagnostic (myelography and discography) and therapeutic (laminectomy) procedures only when a safer, simpler approach fails.

TABLE 1
Possible Contributors to Pain in the Spine
(with or without radicular components)

1. Periosteum
2. Ligaments
3. Muscles
4. Joints
5. Nerve Roots
6. Branches of nerve roots to first four entities

TABLE 2
Disease Processes Capable of Inciting Pain

1. Congenital
2. Traumatic
3. Vascular
4. Degenerative
5. Inflammatory
6. Infectious
7. Neoplastic

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It is obvious from the Tables that a "ruptured" disc represents only a possible cause of pain. An extensive clinical experience suggests that actual disc rupture is a rare event. First of all, ruptured implies a break *through* the annulus fibrosus of the nucleus pulposus. For this to occur, the posterior longitudinal ligament must be at least stretched if not torn. Based upon review of hundreds of patients who have failed to achieve pain relief, and upon several hundred patients who presented with *possible* disc ruptures, I feel that a majority of patients do not have a truly ruptured disc but rather have degenerated discs which may be bulging. Such pathologic entities may be contributing factors but they need not be the *cause* of pain. Thus, the diagnosis of the patient's symptoms is of prime concern.

Pain

Pain may be radicular or focal. Findings of paravertebral muscle spasm, tenderness, limitation of motion, flexion of the back and limited straight leg raising are common.

Neurologic Deficit

Sensory

Subjective numbness is a common accompaniment of pain and may be a reflex phenomenon. True loss of sensation should be segmental, definitive, and possibly progressive.

Motor

Subjective weakness is a common response to pain. Muscle "holding" because of pain may lead to apparent weakness or to apparent reflex changes. Clear-cut muscle weakness is the one symptom which should lead to immediate definitive diagnostic tests; for the lumbar region we personally prefer discography unless there is a clinical suspicion of a tumor. At other spinal levels, myelography is essential.

When there is no significant motor weakness or bladder or bowel dysfunction then there is no need to subject the patient to the discomfort and risk of contrast diagnostic tests unless conservative treatment has reached an impasse.

Conservative Management

Acute—Standard Xrays, general physical exam, and CBC should be done to help rule out fractures, neoplasm, infections, etc.

Bed rest combined with muscle relaxants, sedatives, and analgesics may be prescribed for one to two weeks. During this period heat and external electrical stimulation may offer symptomatic relief. As soon as the patient is reasonably comfortable, ambulation should begin; gentle flexion and extension exercises can be added as soon as possible.

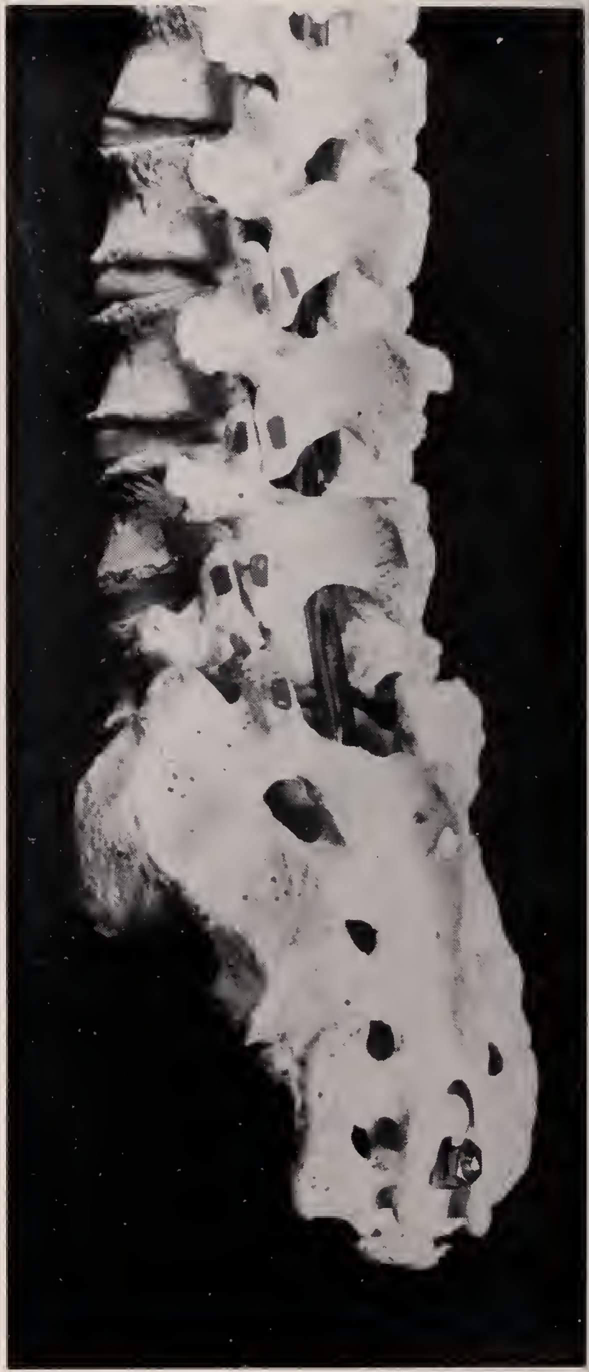

Fig. 1—The gray rectangles mark the facets on this spine model.

Acupuncture

Acupuncture may be of considerable benefit even early in the course of back pain.

Traction

Cervical traction offers relief more consistently than in pelvic traction. If no help occurs within one week, it is unlikely to be of benefit.

Immobilization

Cervical collars seem to be more effective than traction. Lumbosacral supports have limited value. Neither of these should be continued beyond one month unless there is a fracture or dislocation.

Manipulation

In Europe, spinal manipulation is an accepted modality. In properly selected patients it may be the deciding factor in recovery.

Chronic

Once the patient has experienced pain and has been out of work six months, he becomes increasingly resistant to therapy. Thus, whenever possible, a major decision should be made before this length of disability.

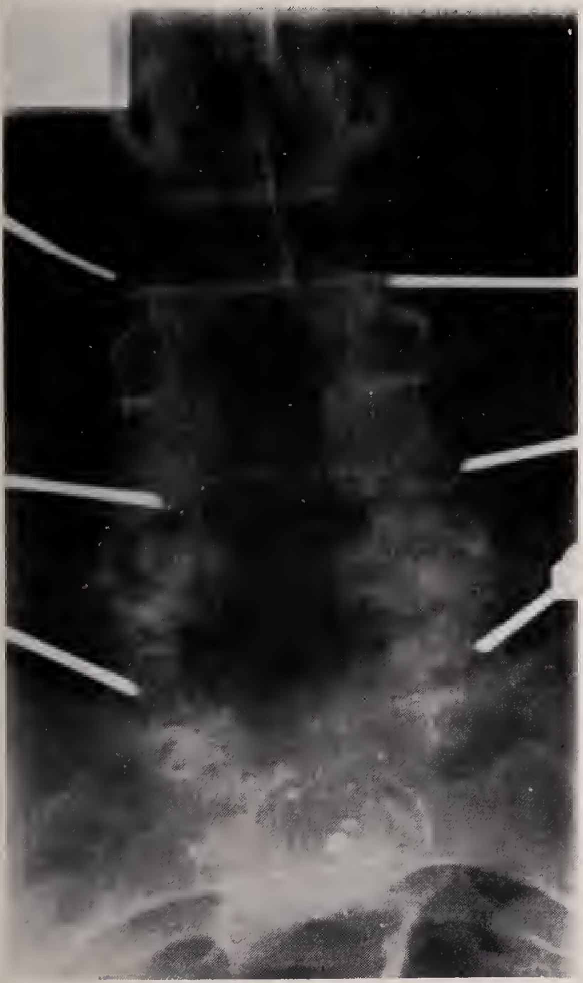

Fig. 2—Six guide needles down to touch facets.

Psychological Evaluation

Chronic pain problems are usually compounded by emotional conflict. Careful analysis of the Minnesota Multiphasic Personality Inventory (MMPI) in back-injured (and chronic pain patients in general) reveals that at least 76% have problems with hysteria, hypochondriasis and depression.[1] Often hostility, paranoia, and other disorders are evident. It is difficult to separate the physical from the psychological. A vigorous approach at behavioral modification (operant conditioning) is a valuable asset in such patients.[6] Acupuncture and external electrical stimulation are valuable adjuncts.

Facet Rhizotomy

The newest approach to the disabling back problem is radiofrequency destruction of the articular nerve supply of the spinal facets (Figure 1). A blind surgical approach to these rootlets was described by Skyrme Rees, an Australian surgeon.[9] After trying this technic in 29 patients and finding a 20% incidence of unacceptable subcutaneous hemorrhage, I reasoned that the small articular nerves could be reached and destroyed by a radiofrequency electrode.

The *rationale* for this approach lies in the fact that facets must be physically altered by any damage to the intervertebral disc. The disc itself has no nerve supply and it can cause pain by disrupting the posterior longitudinal ligament or by pressing against the nerve root. Secondarily, if the disc narrows the facets must overlap more and thus place strain on the joint capsule and its nerve supply. The existence of these nerves has been known for many years even though they have no formal anatomical name.[7]

Technic

Under fluoroscopic guidance 14 gauge thin-walled cannulae are guided adjacent to the centers of tender facet joints. A radio-frequency thermister electrode (19 cm. long, 1-2 mm. diameter) is passed through one needle, the needle is withdrawn, and the electrode is slipped over the edge of the facet and advanced to the intertransverse ligament. A lateral x-ray film confirms the position of the electrode and its distance from the main nerve root (Figure 2).

Electrical stimulation (1 ms pulse width, 25 cps) is applied to the electrode to determine whether there is muscle contracture (electrode too close to main nerve root) and to determine whether such stimulation reproduces at least part of the patient's pain pattern.

A radiofrequency generator (Radionics, Model 3A, Burlington, Massachusetts) is activated when the clinician is convinced a lesion should be made. Temperature is increased to achieve a tip temperature of 80 degrees, electrode left in the central position for 60 seconds; and then the hub is deflected toward the cephalad part of the facet and later the caudal portion of the facet for 45 seconds in each direction. Testing is repeated at all suspected joints (those painful to finger pressure); coagulation is done only if part of the clinical pain complaint is reproduced.

Results

Stimulation of apparently distressed facets routinely reproduces pain in a distribution partially or totally that noted clinically by the patient. Although radicular components of the pain often follow the main dermatomal distribution, only rarely does such pain radiate into the toes. Furthermore, in patients with back pain and no radicular pain, stimulation of the facet rarely evokes spread of pain below the buttocks.

Most commonly one or more facets evoke pain radiating through the back posteriorly through the buttocks, down the thigh to the knee. Such a pattern has been seen from all five lumbar facets (rarely all five in the same patient). Less commonly the evoked pain spreads through the calf to the ankle and quite rarely into the foot. Radiation of pain to the groin or anterior thigh is occasionally seen but it also is not related to any specific facet joint.

In a small percentage of unoperated patients and in 10-20% of patients with fusions, stimulation of a facet provokes *contralateral* pain, demonstrating the tremendous provocation of nerve growth by such massive operative procedures.

Occasionally the electrode has been maneuvered to stimulate other structures, such as the base of the spinous process, the interspinous ligament, or the sacro-iliac joints. Stimulation of all these areas may lead to spreading radicular sciatic pain, but this is rare.

TABLE 3

	Results			
Category	Failure	Good	Excellent	Total
Previously unoperated[1]	6	24	30	60
Previous lumbar surgery[2]	9	8	13	30
Lumbar fusion[3]	25	17	8	50
Total	40	49	51	140

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[1] This is a very mixed group of patients including those with compression fractures, discogenic pain, etc. About half have had a myelogram. At least 10 of these had myelographic defects compatible with a "bulging" disc.

[2] These patients have had one or more lumbar laminectomies for "ruptured" discs.

[3] Many of these patients have had also a clear cut diagnosis of arachnoiditis.

In only two patients who have undergone facet rhizotomy in the past 16 months, has a *ruptured* disc been subsequently removed. Both these individuals had recent trauma (3 months); and, in one, the rupture was strongly suspected although no contrast procedure had been done earlier.

A complication has been a superficial small skin burn secondary to defective insulation on the electrode.

Discussion

It is apparent that back and radicular pain may arise from a variety of anatomical areas and pathologic conditions. When pain is the only major finding and when an apparent pathologic cause is not easily found, one should consider the possibility of a psychological contribution to the incapacity.

Before resorting to laminectomy, or (even) to either myelography or discography, we recommend consideration of radiofrequency facet denervation. The procedure has an amazingly benign record and, especially in virgin back problems, an excellent chance of accomplishing satisfactory pain relief. The greatest concern of this procedure is the possibility that the nerve may regrow. Only two patients, to date have had late (after three to six months) return of pain. Since the nerve has such a short distance to regrow it seems likely that such regeneration would occur within a few months at most. To date no patient has developed increased pain to suggest a neuroma. This could conceivably happen.

There is the question of trophic joint disturbances aggravated by denervation of the facets. Since most of the patients operated already have osteoarthritic changes in the affected facets, it will be most difficult to assess this factor. Serious problems would ensue only if the degenerating joints compromised a narrow bony canal.

Although our experience is more limited in the cervical and dorsal areas, the approach there seems as applicable as in the lumbar spine. Greater caution must be exercised to avoid trauma to vertebral artery or the pleura.

Finally, the most important contribution of facet denervation is to focus our attention on structures other than discs as sources of back pain. Indeed, it appears likely that the majority of back and sciatic pain syndromes are the result of mechanical alterations in the small facet joints. Of over 275 such patients seen in the past year, at least 70% had pain related primarily to facet distress.

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In the middle of the night our hero was wakened by a loud bellowing. It was only King Corny in a paroxysm of the gout. "Pray now," said he to Harry, who stood beside his bed,—"now that I've a moment's ease,—did you ever hear of the Stoics that the book-men talk of, and can you tell me what good any of them ever got by making it a point to make no noise, when they'd be punished or racked with pains of body or mind? Why, I will tell you all they got—all they got was no pity;—and who would give them pity that did not require it? I could bleed to death in a bath as well as the rest of them, if I chose it; or chew a bullet, if I set my teeth to it, with any man in the regiment—but where's the use? Nature knows best, and she says, *roar!*" And he roared—for another twinge seized him.*

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*Maria Edgeworth, **Ormond, a Tale**, 1817.

Cover Painting

"Pain"

Birney Quick, well-known Minnesota artist, muralist and teacher, is a Professor of Painting and Drawing at the Minneapolis College of Arts and Design. At the request of Dr. Walter Indeck, Mr. Quick sketched the ink drawing on this month's cover.

Quick's works have been exhibited in one-man exhibitions at: the Minneapolis Institute of Arts; Walker Art Center; Kilbride-Bradley Gallery, Minneapolis; Tweed Gallery, Duluth; and the Martin Gallery, Minneapolis. His works have been in group exhibitions at: the Minneapolis Institute of Arts; Art Institute of Chicago; Walker Art Center; Tweed Gallery; "Drawings of USA," travelling exhibition sponsored by the American Federation of Art; and the United States Information Service travelling exhibition to Asia.

Quick studied at the Vesper George School in Boston and in 1951 received a B.F.A. degree from the Minneapolis College of Art and Design. He is a winner of the Tiffany Foundation Two-year Fellowship and the Chaloner Foundation Fellowship Second Award. His works are represented at: the Minneapolis Institute of Arts, and the Art Institute of Chicago.

Transcutaneous High Cervical "Electrical Cordotomy"

B. L. CRUE, M.D.* and A. FELSOORY, M.D.†

Report of electrical skin stimulating procedure for the interest of those engaged in either pain research or in treating patients with chronic pain syndromes.

THE FEASIBILITY OF percutaneous high cervical cordotomy has been well documented by Mullan, et al.[23] Rosomoff, et al.[26,27] popularized a lateral approach (Figure 1A), utilizing a radiofrequency lesion. An anterior approach (Figure 1B) was then described by Lin, et al.[17] A posterior approach (Figure 1C) for percutaneous stereotactic high cervical radiofrequency cordotomy was described by Crue, et al.,[11,13] and Todd, et al.[37] Shealy, et al.[31,34] reported that repetitive stimulation of the spinal dorsal column by implanted electrodes (Figure 1D) also effectively decreases pain from lesions below the site of implantation. Crue, et al.,[12] reported stereotactically placing percutaneous paired electrodes in the epidural space of the cervical spinal canal. Relief from pain was obtained by passing a repetitive minimal current through this cervical spinal cord region (Figure 1E).

Shealy, et al.,[29,30,32-35] and Mortimer, et al.,[19-22] have persevered, and along with the dorsal column study group, have demonstrated that relief from pain can be obtained by stimulation of the dorsal column in a larger percentage of patients than perhaps might be expected only from a placebo effect. Shealy's experimental work[28] would lend support to the concept that there is, indeed, a physiological effect caused by stimulation of the large fibers on the dorsal column. This may be related to the "gate theory" put forth by Melzack and Wall.[18] Others such as Wall and Sweet,[39] and White and Sweet[40] have carried out similar experiments using electrical current stimulation of large fiber systems in an attempt to obtain clinical evidence of relief from pain.

In an attempt to verify Shealy's thesis, our group initially utilized epidural paired electrodes placed in the lower thoracic region, threaded cephalad from below at the time of decompressive lumbar laminectomy for metastatic carcinoma (reference,[12] Chapter 7, Figure 7-4). When this appeared to be efficacious, it was questioned if epidural electrodes might be placed higher in patients for alleviation of pain without subjecting them to laminectomy. Epidural electrodes were placed percutaneously in the upper cervical region by means of the Todd-Well's stereotactic machine, in a manner similar to the posterior approach for percutaneous C1-C2 cordotomy (Figure 1E). In one patient (reference,[12] Chapter 7, Figure 7-5), electrical stimulation consisted of a balanced square wave at one hundred cycles per second, 0.3 milliseconds duration, and amplitude of three to eight volts. Surprisingly the patient could tolerate higher voltage, but seemed to have both suppression to pin-prick caudad and clinical relief of pain from her "frozen pelvis" (due to carcinoma of the cervix) using lower voltage, the optimum being approximately four to five volts. The patient had been terminal and had been maintained on large doses of morphine sulphate (up to 30 milligrams every two hours). No further morphine medication was needed after electrical stimulation was started. The electrodes were left in place for sixteen days and were then removed because of the possibility that they might introduce infection and lead to an epidural abscess. The patient continued to be free of pain after the electrodes were removed. She never developed any sign of infection or cervical cord damage clinically, and survived for twenty-three more days.

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Instead of trying to find a way to anchor more securely paired electrodes introduced percutaneously into the epidural space (so that the patient could be ambulatory without danger of damage to the cervical cord) it appeared that the next logical step should be an investigation of the effect of repetitive electrical stimuli on the spinal cord in the cervical region if the stimuli were applied transcutaneously.[8] This procedure (as illustrated in Figures 1F and 1G) has now been carried out in nine animals, five human volunteers, and forty-eight patients with chronic pain due to both malignant neoplasms and chronic benign pain syndromes, between April, 1970 and September, 1973.

Technique

The skin surface electrodes are placed on either side of the neck, over the tips of the C2 transverse spinus processes, approximately one inch below the tips of the mastoid. We soon discarded the constrictive rubber band around the neck initially used to hold the electrodes in place. Instead, various types of electrodes and electrode pastes were investigated. At this time, the preferred type of electrode placement is shown in Figure 2 where

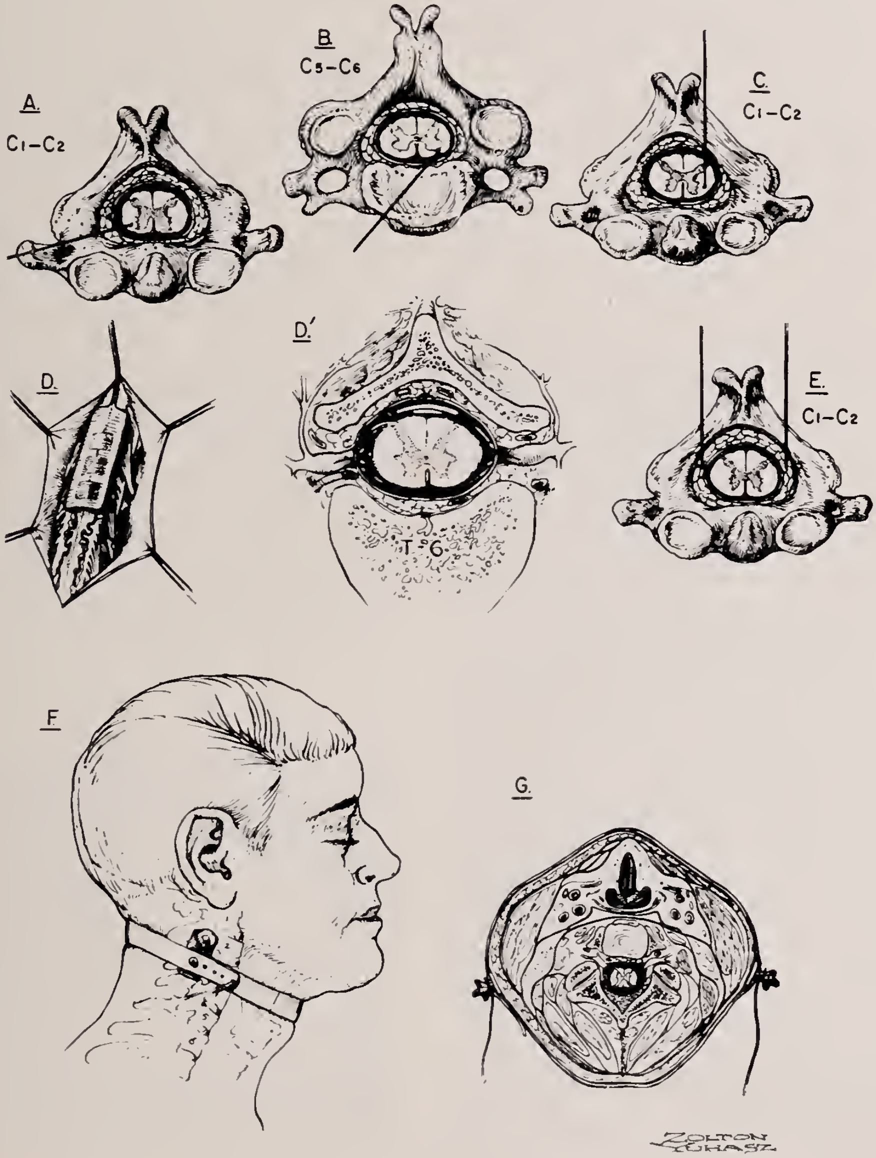

Figure 1

our research secretary is modeling our present portable apparatus. The electrode wires have a coupling that can be disconnected easily by the patient. The portable stimulating unit, which is battery powered, is carried in a sling over the shoulder. The parameters of the stimulator were standardized at 100 Hertz and a balanced square wave of 0.2 milliseconds duration. The one variable in the stimulator is the voltage. The amplitude may be adjusted by the patient, or if he is not physically or mentally capable of this, then either the technician, nurses or physicians can alter the voltage. To diminish the weight and the cost of these portable stimulating units developed at City of Hope, the current read-out is obtained by a separate unit. It is carried to the patient's bedside by the physician on daily rounds and plugged into the stimulators (Figure 3). This unit gives a direct "read out" of voltage being supplied and the milliamp current flowing between the two electrodes. The time of application was also an arbitrary decision. The patients were at first given only a few hours stimulation. When this procedure had been shown to be clinically safe, the patients were given 24 hour, then 48, 72, and finally 96 hour runs. Several of our patients have had repeated four-day trials with this stimulator and demonstrated no evidence of organic damage to either the neck or the spinal cord. (At first there had been some skin damage with the original EKG metal plates; but, then in the last two years, the only skin problem has been an irritative dermatitis that cleared promptly after removal of the electrodes.)

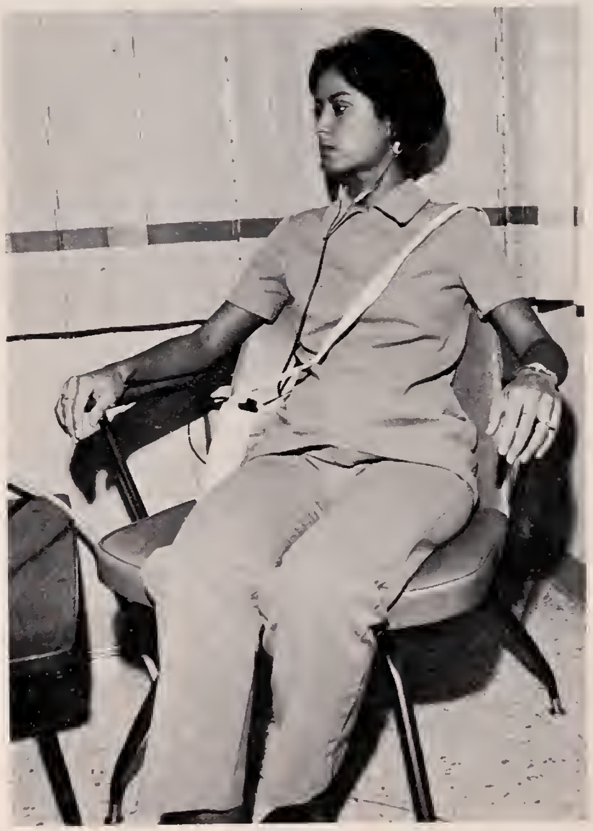

Figure 2

Subjects

Of the 48 patients, there were 30 female and 18 male. They ranged in age from 16 to 79 years. Twenty-nine were treated for pain from terminal malignancy, including 12 patients with cancer of the breast. Nineteen were done for benign chronic pain conditions of various types, including seven who had continued pain after failure of multiple lumbar laminectomies. There were no double-blind controls carried out in this series. There were nine patients where a sham procedure was tried initially (without any current); and, there were two cases that had dummy-paired electrodes applied (so that the current was applied only through the skin of one side of the neck, instead of through the neck itself).

Results

Only 15 of the 48 patients (or 31%) obtained significant clinical (full or partial) pain relief, even of short duration.[14] Six of these were patients with cancer, and nine had a chronic benign pain syndrome. Three patients with phantom limb obtained relief, and this seemed to indicate that this was probably the single most favorable pain condition in our series for which this procedure was applied. There were several patients who

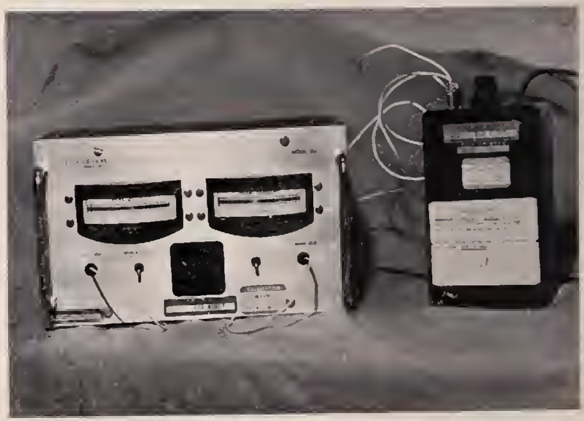

Figure 3

seemed to obtain prolonged benefit from this procedure. One patient with phantom limb obtained complete relief by the electrical current, and the pain relief lasted for many days after the current stopped. Another patient with a thoracic spinal cord injury (Brown-Séquard syndrome)* went many months with complete relief of pain between electrical stimulations. One elderly male patient with chronic sciatic pain following unsuccessful lumbar disc surgery has gone back to managing his ranch, and is maintained relatively pain free by using this stimulating technique for a few minutes at a time two or three occasions a week.

Discussion

The reaction to electrical stimulation was quite variable. The patients with cancer, who were on narcotics, seemed to have the highest pain threshold, and could usually tolerate the most electric current. There was no evidence from this small series to indicate that pain relief clinically was in any way quantitatively related to the amount of milliamps that we were able to administer through the cervical region. The local electrical effect caused painful spasms in the cervical muscles (including the trapezius), and was a limiting factor in the treatment of most patients. In many patients with anxiety, fear of the electric current caused some of the patients initially to tolerate only a very low current. Often, after a few hours trial, the milliamperage could be increased appreciably. The variation from patient to patient in skin resistance was surprising, and more variable than that usually seen from time to time in the same patient. The least ma. that could be tolerated was approximately one milliamp, and some patients tolerated as high as 35 milliamps. The individual variation in resistance was illustrated when one patient at 12 volts had only one milliamp flowing, while another patient in an identical room with an identical apparatus stimulated at three volts had 15 milliamps passing through the neck.

Logical consideration would lead to the conclusion that, if this procedure is indeed clinically efficacious, five possible mechanisms of action should be examined:

1. It may all be due entirely to suggestion. There can be no denying the fact that relief from pain, even in terminal cancer patients who seem to be experiencing extreme suffering, can be brought about by the placebo effect alone. This has been well demonstrated by workers such as Beecher.[1] (One of our cancer patients had significant relief from pain that lasted several days following the application of electrodes to her neck. No current was delivered whatsoever!) Besides being based on a statistically insufficient sample, this present series also points out the weakest point of any subjective study. There is no satisfactory end point ,and no really objective means of evaluation. Thus, a double blind study would seem mandatory. The conclusion that the present technique may be efficacious largely, if not entirely, due to suggestion, does not invalidate it as therapy. Even if it is a placebo, it is certainly easier on the patient and the surgeon than a laminectomy for electrode implantation.

2. Another possible explanation for the observed relief from pain is an effect through repetitive dorsal root input into the cervical region, and the "competitive" effect that it may have on the upward flow of impulses originating in pathological areas more caudad. The effect of diverting attention phenomena (such as by acupuncture or mustard plaster application to the chest) is well known. The observation that local anesthetic blocks in the neck can presumably decrease the input into the cervical cord and may make the patient "numb" on that side of the body below the neck area has previously been presented by Crue and Sutin.[10] The effect of sending impulses over the low threshold, large, phylogenetically new, fast fibers, "closing the gate"[3,18,39] has also been discussed previously.[5,7,9] We have recently attempted in the laboratory using cats, and in the human during posterior approach cordotomy,[11] to monitor changes of upward flow in the spinal spinothalamic tract from the effects of a secondary stimulation of dorsal inputs at a level higher than an evoking stimulus in a lower extremity; but, so far, these experiments have been inconclusive. The lack of experimental data from the laboratory, however, should not negate observations made during empirical clinical trials. For example, one of the present authors (BLC) began in 1958 to experiment with peripheral nerve non-painful electrical stimuli in animals (on the trigeminal nerves of

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*See page 209.

cats). This work was extended to patients with pain syndromes (with Drs. Shelden, Pudenz and Todd) at the Huntington Research Institute, Pasadena, California. While physiological rather than electrical stimuli were found at that time to be a better source of "competitive" sensory input, we were able to obtain excellent clinical relief from pain in a majority of post-herpetic neuralgic patients by the judicious use of a portable home hand vibrator, ice cubes, or ethyl chloride spray.[38] Subsequently, by the addition of tranquilizers, and especially the tricyclic antidepressants (Triavil), we no longer consider, post-herpetic neuralgia a suitable operative conditon. The few remaining intratable post-herpetic pain patients have so many central, or frankly psychiatric, potentiating factors that only central operative approaches effecting "affect" may be indicated.

3. Another possible explanation may be that there is a direct effect of minimal electrical currents from the present transcutaneous electrical cordotomy on either the long tracts in the cervical cord, or on the neurons in the cervical cord, probably in the dorsal horn substantia gelatinosa "computer complex". The effect of low current electrical stimulation from electrodes on the skin surface has been described often in the literature, but usually from the standpoint of changes in circulation or muscle.[2] If minimal repetitive current can directly effect the low threshold large sensory fibers in the dorsal column of the spinal cord, it may do so by stimulating the initiating increased sensory input cephalad for competition with the more "natural" pain information ascending from below, or by initiating more central mechanisms to feed back centrifugal efferent modulating inhibiting mechanisms. The stimulated dorsal column fibers may also conduct antidromically caudad to block pain impulses at the dorsal horn gate at the lower "painful" segments. If the long sensory tracts are stimulated, the stimulation may be carried in either the dorsal columns[25] or the smaller fibers in the spino-thalamic tract in the anterior quadrants of the cord. If the larger fibers with the lowest thresholds are all equally in the line of electrical current flow, we cannot explain the fact that no motor movements have been produced by stimulation of the large low threshold fibers of the pyramidal tracts[36] in these patients undergoing transcutaneous stimulation. If the minimal currents act instead directly on the neurons, or their dendritic standing potentials, in the electrical field of the stimulating electrodes, the effect may be on the reticular neurons involved in the Noordenbos[24] "chicken wire" concept of the phylogenetically old slow component for ascending pain information. Alternately, the electric current may act on the "T" cells of Melzack and Wall[18] in layer five of the dorsal horn, or on the "S.G." cell in layers two-three, or on the "A" cell of Christensen and Perl,[4] in the most superficial layer, that may be more specifically related to "pain."

4. The electrical effect may be entirely chemical, e.g., an effect on the chloride ion concentration as suggested by the work of King et al.[16] studying the effect of Hitchcock's technique[15] of subarachnoid injection of cold hypertonic saline in patients with pain. The cumulative effect of 24 hours of stimulation at 100 Hertz equals 8,640,000 shocks, and certainly deserves further study.

5. The last logical conclusion might be that perhaps there is a combination of any or all the above mechanisms of action working in "summation". Of course, there are probably other possibilities, such as local hypoxia from electrically induced changes in vascular supply. In theory, all of these suggested explanations are capable of experimental verification.

Conclusion

It is the authors' impression that the results in pain relief obtained in this study at the City of Hope[6] are largely, if not entirely, due to placebo. The element of suggestion, and the effect of decreasing the patient's anxiety, cannot be overemphasized in the treatment of patients with chronic pain. This electrical skin stimulating procedure is being reported for the interest of those engaged in either pain research, or those treating patients with chronic pain syndromes. It is not being advocated as a demonstrated useful adjunct in many cases. In the future, we intend to use this procedure only as one part of our armamentarium. It may well prove that electrical current may be more effective if it is introduced into the human cutaneous afferent system in regions nearer the painful areas, as has been suggested by workers such as Shealy and Long. It is believed that our attempts at electrical stimulation are certainly more conservative than operaive intervention, regardless of what type and at vhat level, and certainly this present technique leserves further clinical trial before subjecting patients to the risk, discomfort, and expense of more radical neurosurgical procedures.

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Brown-Séquard Syndrome

The features of this syndrome consist of homolateral motor paralysis and loss of deep joint, tendon, and vibratory sensation, with contralateral subjective loss of pain and temperature below the level of a lesion of the spinal cord. Tactile and discriminatory sensibility may be preserved. Brown-Séquard, the French-American neurologist, in 1855 first described the neurologic sequelae of this syndrome after an exact hemisection of the spinal cord in an animal.

Clinically, the syndrome is rarely seen in its complete form. More commonly a partial form occurs as a result of trauma or compression by tumor. The ensuing neurologic findings are variable, depending upon the degree of involvement of the tracts of the cord.

Durham, Robert H.—Encyclopedia of Medical Syndrome
Hoeber Medical Division, Harper and Row, New York

Implantable Electrical Devices for Pain Relief

DONALD ERICKSON, M.D.* and SHELLEY CHOU, M.D.†

Implantable dorsal column and peripheral nerve stimulators have been used for relief of chronic pain at the University of Minnesota Hospitals for the past four years. A review of the long term results shows that patient preparation and selection are major factors in determining success or failure. Strict selection criteria have now been established which we believe will allow continued use of these devices with acceptable results.

THE USE OF IMPLANTABLE electrical devices for the relief of chronic pain has been an area of active clinical investigation over the past five years. There is a great deal of controversy regarding the value of these devices and to date, no well-documented reports have been published. This discussion summarizes our experience at the University of Minnesota Hospitals and illustrates present policy regarding the use of these devices.

Theory of Electrical Stimulation for Pain Relief

Melzack and Wall initiated a new line of clinical activity for relief of chronic pain by electrical stimulation when they proposed the "Gate Theory" of pain transmission in 1965.[3] This theory describes a spinal cord modulating mechanism whereby one type of sensation such as light touch or vibration can impede the transmission of another sensation such as pain. It is known that sensations such as light touch are transmitted by the larger, more rapidly conducting fibers in the peripheral nerves, which would reach the spinal cord sooner than the slower conducting smaller fibers which transmit painful impulses. Reaching the spinal cord first, they can activate a pool of modulating neurons and blockade the incoming pain signal. Electrical nerve stimulators have been developed which can readily activate the large fibers producing a tingling or vibratory sensation, thereby blocking noxious or painful stimuli.[7,8]

It is known anatomically that the dorsal columns carry the majority of light touch and vibratory sense to higher centers, and the idea was conceived that perhaps one could stimulate the dorsal columns directly and achieve a broader area of stimulation and pain relief. Other investigators have turned their attention even more centrally to the thalmus, and have devised methods of electrode implantation and chronic stimulation for pain relief. The following is a brief review of the present implantable devices that are being used clinically in an attempt to relieve pain.

Description of Implantable Devices

There are basically three types of implantable electrical devices now being used. The dorsal column stimulator (DCS) was first used clinically and reported by Shealy in 1967.[4-6] This device consists of an electrode which is implanted in the spinal canal over the posterior aspect of the spinal cord and connected to a lead wire which runs subcutaneously to a receiving unit. This unit is composed of an induction coil and electrical circuit capable of generating a current when activated transcutaneously with a radio frequency transmitter and antenna. The patient then perceives tingling or vibratory sensation in the trunk and extremities capable of blockading pain sensation in the same area. The second type of device is a peripheral nerve stimulator (PNS) comprised of an electrode placed around a peripheral nerve and similarly attached to a lead wire and receiving device. When activated, the patient perceives a tingling or vibratory sense in the distribution of this nerve which is capable of relieving pain located in that area. The third type of device is a thalamic electrode, which is implanted stereotactically and activated by a similar mechanism.[1] We have no experience at the University of Minnesota Hospitals with this latter device and this report will be concerned primarily with dorsal column and peripheral nerve stimulation.

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Patient Selection

It has become evident over the past several years that perhaps the most difficult part of using the implantable electrical devices is proper patient selection. Patients who are involved in major litigation or compensation suits, patients who have a hysterical basis for their pain, or patients who are having severe problems with drug abuse or drug dependency are, in general, poor candidates for any type of surgical relief of chronic pain. Our goal at this time is to select patients who have no significant secondary gains related to their pain problem or to the proposed operative procedure, and who would be able to make a significant change in their activity level and life style if the implantable device could relieve their pain. These judgments are difficult to make so we have established the following criteria which must be met:

1. established physiological basis for their pain which could not be adequately treated by standard surgical or neurosurgical methods.
2. no major psycho-pathology as determined by clinical appraisal and MMPI testing.
3. a relatively stable social setting including such things as marital status and financial status.
4. reasonable and rationally established future goals regarding activity levels including such matters as employment potential.
5. freedom from any drug abuse especially narcotics and barbiturates.
6. a favorable response from some form of electrical stimulation on a diagnostic trial.

We do not expect that the majority of chronic pain patients will have fulfilled these criteria when we first start our evaluation. We therefore have an inpatient program which includes: drug detoxification, physical reconditioning, psychological and vocational counseling whereby we attempt to help the patient meet these criteria. It has been our experience that many patients, after meeting these criteria, no longer need surgical intervention and are therefore discharged without implantation. Many patients have such an emotional content to their pain problem that when this is corrected, the level of their pain is no longer unbearable or incapacitating. This aspect of patient care will not be dwelt upon, as it is covered more comprehensively in other papers dealing with operant conditioning and behavior modification.[2]

Description of Diagnostic Electrical Stimulating Techniques

These techniques, relate specifically to the implantation of pain relieving devices, and will be described in some detail. We have available, small flexible electrodes which can be inserted through a 17 gauge needle into the spinal column adjacent to the spinal cord or into an extremity adjacent to a major peripheral nerve. For insertion of the peripheral nerve electrode, local anesthesia is used and the nerve is located by producing parathesias with the 17 gauge needle. Once the nerve has been located, the electrode is inserted through the needle adjacent to the nerve and taped to the skin. The electrode is then connected to a stimulating device and left in place for one or two days. The patient has control of the stimulating device and is able to determine whether or not he can adequately control his pain by electrical stimulation. The institution of the diagnostic intraspinal electrodes requires fluoroscopic control and is somewhat more difficult. A spinal puncture is made at the upper lumbar or second cervical level and the electrode is then introduced through the needle into the subarachnoid space and manipulated under fluoroscopic control to a desired level over the dorsal columns of the spinal cord. This similarly is fixed in place and connected to an external stimulating device. Once again, the patient controls the level of stimulation and is able to determine over the next day or two whether this stimulation gives him adequate pain relief. If the patients respond favorably to this type of stimulation and has met the other criteria, they are then candidates for implantation of a permanent device.

Clinical Materials and Results

We do not intend to present a detailed review of all results at the University of Minnesota Hospitals in the use of these devices, as we are still in the process of evaluation at this time Over the past five years there have been many changes in the electrode design and in the techniques of implanting electrodes which will make it very difficult to make a definitive evaluation of the procedure. In addition, the patient selection methods have changed considerably so that many patients done in the past would not be considered acceptable candidates at the present time. An attempt will be made to give a general summary of what has been done and our results based on evaluation to date.

A total of 76 patients have undergone implantation of dorsal column stimulators. Seven of these patients had metastatic carcinoma and have subsequently expired. Their results will not be included in this report. Four patients have not been adequately evaluated to date and will also be deleted from the results presented. Of the remaining 65 patients, 25% were technical failures which means that they did not get adequate stimulation over the entire pain area, they had excessive unpleasant stimulation at the electrode level, their stimulator stopped working or, infection required removal. We are not able to state at this time whether or not these all represent a failure of instrumentation or if perhaps some idiosyncracy in the patient's response may have doomed him to failure regardless of the technical system. An additional 49% of patients were failures based on inadequate relief regardless of the stimulation produced. This includes patients with functional overlay who may have initially responded well but made no subsequent objective signs of improvement, and also patients who claimed pain relief in the previous pain area, but developed new pain areas. This leaves 26% of patients who have what we consider a good result. By good result, we mean that the patient does not use narcotic analgesics and has demonstrated significant pain relief by making an objective improvement in his life style. When one considers that this entire group of patients was refractory to all other methods of pain relief, this relatively small percentage of success may still be considered acceptable. In the past five months, utilizing the new selection criteria and a new electrode design, we have performed implants on seven patients, all of whom are receiving good stimulation and fair to good pain control. We have reason to believe, therefore, that with improved understanding of pain patients, and further technological advances, we will have better results in the future.

Seventeen patients have undergone some form of peripheral nerve stimulator implantation. Four of these patients had specific peripheral nerve injuries and had excellent relief of pain with implantation of a stimulator on that particular nerve. Five patients had implantation of sciatic nerve electrodes for relief of back and leg pain which was due to herniated disc and multiple operative procedures. Two of these patients have had good pain relief of both leg and back pain. This demonstrates that it is possible to relieve pain by peripheral stimulation even though the offending lesion is proximally located. The remaining eight patients had a variety of problems such as cauda equina injury, amputation stump pain, phantom limb pain, and brachial plexus injuries. Two of these patients were benefitted by the procedure. The results are not overwhelmingly successful, but again, one must consider that most of these patients had undergone multiple previous operative procedures in an attempt to relieve their pain. Implantation of the peripheral nerve stimulators is safer and easier than implantation of dorsal column stimulators and we are continuing active investigation of its use.

Summary

This article represents a preliminary review of the patients who have undergone implantation of dorsal column or peripheral nerve stimulators at the University of Minnesota Hospitals during the past four years. This review has made it evident that the failure rate will be high in this group unless one is able to resolve the attendant drug dependency, psychological, and sociological problems that are concomitantly present in patients with chronic pain problems. Improvement in technology along with our present patient preparation and selection criteria give us reason for enthusiasm regarding the potential of electrical stimulation for pain relief. We remain reserved in our judgment regarding use of these devices at the present time and believe it will take several more years to adequately determine the ultimate value of electrical stimulation for the treatment of intractable pain.

References 1-8 will be found on page 228.

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nd for prolonged relief.

Lacking in substantial evidence of effectiveness: For relief of nasal
congestion and hypersecretion associated with the common cold and
inusitis.

Final classification of the less-than-effective indications requires further
nvestigation.

ontraindications: Hypersensitivity to any component; concurrent MAO
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hildren under 6.

Varnings: Caution patients about activities requiring alertness (e.g.,
perating vehicles or machinery). Warn patients of possible additive effects
ith alcohol and other CNS depressants.

sage in Pregnancy: In pregnancy, nursing mothers and women who
ight bear children, weigh potential benefits against hazards. Inhibition of
ctation may occur.

ffect on PBI Determination and I^{131} Uptake: Isopropamide iodide may
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recautions: Use cautiously in persons with cardiovascular disease,
laucoma, prostatic hypertrophy, hyperthyroidism.

dverse Reactions: Drowsiness, excessive dryness of nose, throat or mouth;
ervousness; or insomnia. Also, nausea, vomiting, epigastric distress,
iarrhea, rash, dizziness, weakness, chest tightness, angina pain, abdominal
ain, irritability, palpitation, headache, incoordination, tremor, dysuria,
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Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: ***Lomotil is contraindicated in children less than 2 years old.*** Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. *Liquid,* 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

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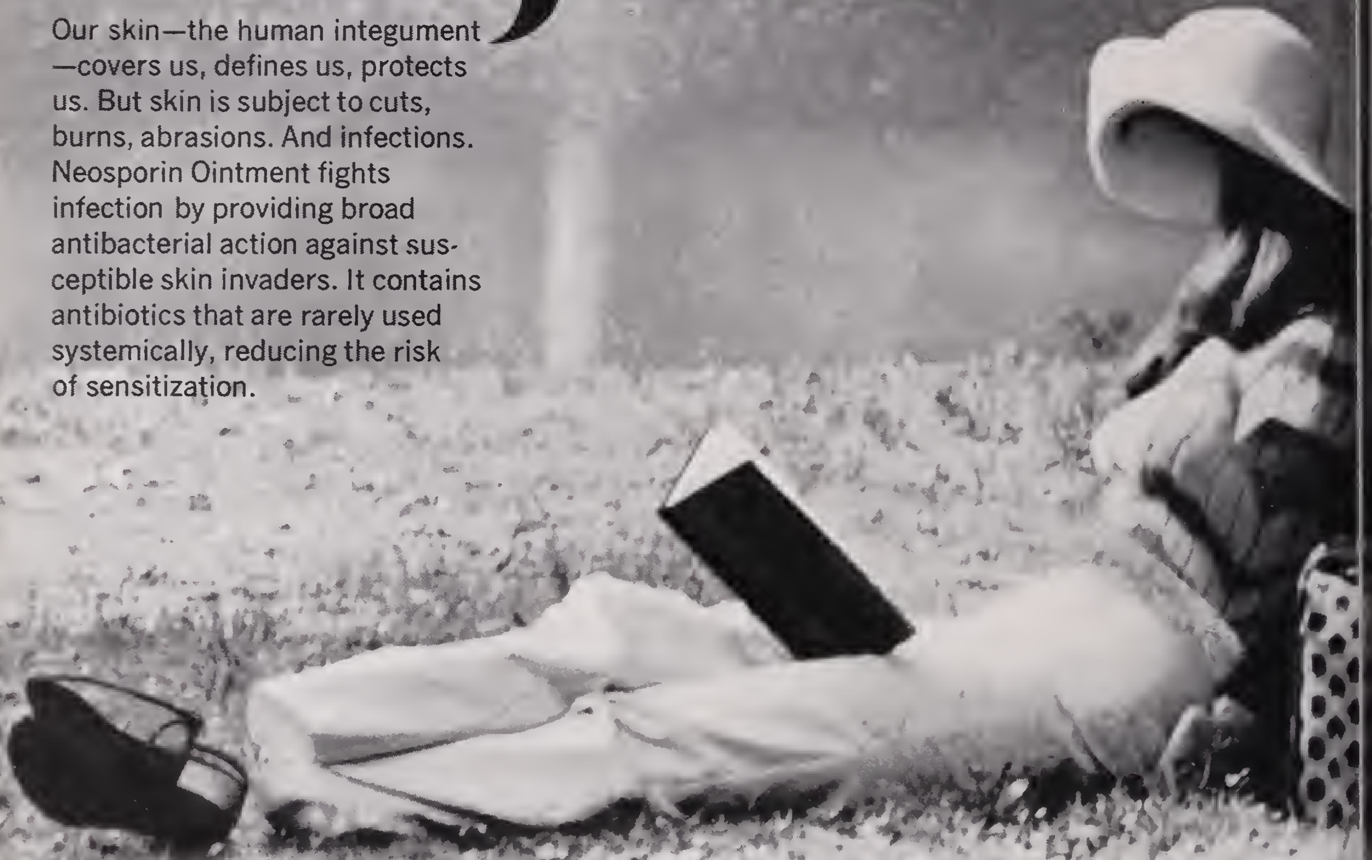

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Editorials

1 + 1 = 1
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COMPUTER LANGUAGE would describe nerve stimulation in its "all or none" behavior by the above formula. Once a nerve is excited, an added similar stimulus does not change the "firing" pattern. If a nerve is inhibited, further inhibitory influence cannot produce a more "negative stage."

It is not possible to explain pain, its interpretation, and its effect so simply.

Chronic pain conditions befall millions of patients and challenge the ingenuity of most physicians. The cost for analgesic medication in the U.S. for 1972 was 1.2 billion dollars. The cost to industry in loss of work time and the cost of medical care when added to this figure becomes a mind-staggering sum.

Imagine yourself as a patient:

> Experiencing the pain of an abscessed tooth for a year—or experiencing the pain of a progressive tumor of the femur for a year.
>
> Then, add to this picture the impact of what these conditions would mean to your work efficiency, need for medication, family interrelationships and outlook for the future.

Most lacerations heal uneventfully; most fractures become painless in a matter of weeks; most peptic ulcers respond to medical or surgical programs, but what of the patient who has had phantom limb pain for twelve years or one who has undergone six unsuccessful operations to relieve low back pain? These chronic pain situations linger, fester, and may create irreparable physical and emotional situations. It is this problem of chronic pain to which we are addressing this Special Issue.

> Increase theta wave output from the brain and diminish pain—"witchcraft" you say.
>
> Apply an electrode to the elbow area and diminish back pain—"balderdash" you say.
>
> As far-fetched as these techniques may sound, reliable investigators have reported dramatic and sustained improvement in patients who have been treated with such modalities.

Analgesic medication is probably considered first in the control of chronic pain, but other techniques may be adjuncts or alternatives:

> Operant conditioning: Programs designed to gradually change the usual gains—or end results—of a patient's habit pattern response to pain.
>
> Bio-Feedback Program: The use of brain wave, temperature modifications, or muscle training programs to diminish pain.
>
> Neurosurgical Procedures: Have been designed to interrupt neural pathways from receptor organ to postcentral gyrectomy.
>
> Electro-analgesia: Has been refined so that it can be applied to a distribution almost as extensive.
>
> Acupuncture.

Experts in these fields have offered their experience and information to use in this issue. Some of these subjects are of such nature that information does not necessarily reach the usual medical journals. The dramatically fascinating control of autonomic system function by individuals such as the Swami Rama have not been widely read, yet techniques such as these may become adaptable to treatment of medical conditions. Medical information may take months and sometimes years to filter from the subspecialty journals; we have been very fortunate to have their articles available for a single issue. To these authors we are thankful for their gracious acceptance of a task designed to keep our information current.

It may be tempting to define all components of pain and prescribe a program directed to overcome each ingredient. Chronic pain has frequently encompassed other factors and a rote prescription becomes ineffective in titrating each aspect to normality. In such instances the "art" of medicine is the secret ingredient for the success or failure of the recipe.

Walter Indeck, M.D.
Guest Editor

The Pain Issue

Ah, thought I, thou mourn'st in vain!
None takes pity on thy pain:
—Richard Barnfield,
Poems in Divers Humors. 1598.

PAIN IS PROBABLY the most important and most feared symptom of human illness. Many patients fear pain more than death, as for instance, cherishing a tumor to its destructive termination rather than accepting the "pain" of an operation.

Among the obligations of the doctor, relief of pain is second only to postponement of death. This March, 1974, publication of MINNESOTA MEDICINE is an inquiry into the present status of methods of pain relief: ancient, modern, and hypermodern (to borrow a chess term whose meaning is obvious).

The cover painting is an artist's conception of the appearance of pain. Severe, acute pain may indeed be obvious to an artist or physician by the contortion of limbs and features of its victim but often these "objective" findings are lacking, and pain is quantified by the statement of the patient. But we are not without other means of assessing severity. Establishing the diagnosis of the painful condition is obviously of first importance. Psychiatric and neurotic factors must be evaluated. The presence of an operant (to use a hypermodern expression) influence may make pain a pleasure, so to speak, as in legal cases where the more the pain, the greater the settlement. Physicians should be aware of the possibility of their reinforcing perpetuation of pain as Fordyce points out.

The gate theory of pain postulated by Melzack and Wall[1] in 1965 offers a neat mechanism that may play a role in hypnosis, counter-irritation, electrical stimulation and acupuncture. Several papers in this issue describe this theory.

Acupuncture is currently in fashion, and there seems to be no question that it can relieve pain even as severe as that of major surgery. But the "explanation" in terms of "meridians" and "Yin" and "Yang" reads perilously close to science fiction.

Several articles are concerned with back pain reflecting the special interest of the Guest Editor, Walter Indeck. Dr. Indeck has referred to the non-mathematical concept that 1 + 1 = 1. In Medicine such mathematics as 1 + 1 = 2 need not always apply. Thus, one symptom: pain; plus one surgical diagnosis: ruptured nucleous pulposis; does not always add up to two, an operation (or for that matter five or six operations as described by Long). This analogy wanders somewhat off the mathematical mark, but will be understood by the profession.

Indeck, and the many authors who have responded to his request for articles for MINNESOTA MEDICINE, have made important contributions on the subject of pain, important to all physicians interested in pain; that is to say, all physicians.

Reuben Berman, M.D.
Editor

Reference

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Dr. E. Starr Judd and the Mayo Enterprise

When I learned that my good friend, Waltman Walters,* was scheduled to speak of Dr. E. Starr Judd and his career at the Mayo Foundation House on the evening of July 11, I realized it would be an event that would stir pleasant past memories and an occasion one could not afford to miss. These quarterly sessions in the History of Medicine, held at the Mayo Foundation House, the great house in which Dr. and Mrs. William J. Mayo lived and in which, over many years, they extended cordial hospitality to many friends, has captivating recollections for all fortunate enough to have been privileged to savor such occasions.

It was indeed a great evening in which Dr. Walters underscored the salient features accountable for Dr. Judd's unique success as an operating surgeon and his recognition as one of the great American surgeons of his time. Dr. Judd was among the first additions to the Mayo surgical staff. He was a native of Rochester and a graduate of the University of Minnesota's Medical School (1902), followed by an internship at St. Mary's Hospital in Rochester. Dr. Judd lived not far from St. Mary's Hospital and consistently walked to and from his home. We, his residents, met him at the entry at 7 o'clock and proceeded immediately to accompany him on his morning visit to his numerous patients, scattered widely about on various floors and segments of the hospital. As we hurried along the corridors of the wards, it was the special function of the residents to acquaint Dr. Judd with the current situation of each patient, for we had been up at 5 a.m. to visit the nursing stations to garner first hand information regarding the status of all patients to be passed on to Dr. Judd during this marathon.

Sister William was Dr. Judd's operating supervisor. Her whole life was devoted to Dr. Judd and his patients. Whenever we visited the operating rooms prior to our early morning nursing station visits, Sister Bill, as she was affectionately known to all surgical residents, was already on the job getting things organized for the day's work. On Sunday afternoons, she could regularly be seen visiting Dr. Judd's patients. Dr. Judd did have an unusual facility to evoke the finest sense of loyalty from all his associates.

Dr. Judd had an obvious reserve, only susceptible of ready penetration upon topics or questions of immediate or direct concern. He apparently was constantly preoccupied by matters relating to professional aspects of the day's schedule. The care of his patients was always uppermost in his mind. Dr. Judd had a tremendous background of knowledge and experience in the broad areas of his special concern and activities, readily and fully shared and discussed at an appropriate moment, with his residents. Only in the bosom of his family or with close friends among his professional associates was Dr. Judd known to shed his external constraint, an inference nicely supported in Dr. Walter's interesting account.

Dr. Judd was a careful and astute observer. Nothing relating to patient care escaped him. He was gentle but firm in all his dealings with his house officers. As one peruses his nice bibliography, it is quite evident that Dr. Judd lent encouragement and provided the needed incentive for his associates to join him in publication. A number of the Clinic's great surgeons including Walter Sistrunk, John Pemberton, Stuart Harrington and Fred Rankin, in their early years, had been a part of the Judd Team. Dr. Judd had a succession of fine first assistants during my year's tenure at the Mayo Clinic, who later became able representatives of good surgery in communities in which they took up their abode. Dr. Walters has nicely sketched how Dr. Judd was able, through the simple device of having two surgical teams, to do a large number of major operative procedures in a single morning.

Dr. Judd's devotion to surgery and self-imposed discipline in the constant acquisition of knowledge and experience were the mainsprings that brought his extraordinary surgical talent and versatility to the attention of his associates and the surgical profession. Dr. Judd's approach to problems was direct. There were no flourishes. He was never hurried, but his intimate knowledge of the anatomy of a large number of surgical procedures, together with undeviating straight forward simplicity in dissection were some of the attributes that made him the great surgeon he came to be. Dr. Judd did not distinguish himself as an innovative surgeon. He strove continuously for perfection in execution of operative procedures and rarely was it possible to detect even traces of flaws in their execution. His intent was to provide the last rather than the first word in the methodology of operations.

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*See page 234.

Dr. Judd was the only clinical surgeon during my stay at the Mayo Clinic who took a keen interest in following the distinguished work of Frank C. Mann at the animal farm and research laboratories, a few miles distant from St. Mary's Hospital. When Dr. Judd's operative schedule was a little lighter than usual he would take his assistants out to spend a few hours observing and discussing with Dr. Mann the nature of problems upon which he was engaged. During that period in time Dr. Mann was wrestling with the problem of assessing liver function and ascertaining how much liver was actually necessary to carry on its normal functions. Perhaps no one since the time of Claude Bernard had addressed himself so vigorously to studies of liver function as did Frank Mann. Dr. Judd recognized fully, as did Will Mayo, the importance of research for progress in all of medicine, including surgery. In Mann's early years at Mayo's he occasionally co-authored papers on the biliary tract with Dr. Judd.

The following episode is illustrative of Dr. Judd's great versatility. One of his patients whom I remember very well was a woman who came from Baltimore, who had been operated upon six times for persistent vesico-vaginal fistula by the eminent Hopkins' gynecologist, Dr. Howard A. Kelly. Said the lady, "Dr. Kelly was a very religious man and on the occasion of my last operation he prayed on his knees on the floor of the operating room for the success of the procedure." Even so, the operation failed. Dr. Judd's nice exposure of the communication between the trigone of the bladder and the vagina made secure closure of the fistula a certainty.

He established the Judd lectureship in surgery at the University of Minnesota which has provided the opportunity for the Department to have annually as its guest a succession of the greatest amongst American as well as foreign surgeons over a period of 40 years. My surgical colleagues and I at Minnesota take pride in the circumstance that Dr. Judd's son, Edward, today a prominent senior surgeon at Mayo's, had spent several months in our surgical clinic at the University. He was the Judd Lecturer during my terminal year (1967) as Chairman of the Department.

Will Mayo was a peerless judge of men. He took great pride in the circumstance that Dr. Judd was a more talented operating surgeon than he. In anatomizing the success of the Mayo Enterprise, several important items emerge. Fundamental to its uninterrupted progression through the perils and entrapments of constant change has been the selection of key persons of extraordinary ability for staff positions with provision for unusual opportunity without any suggestion of intrusion other than timely encouragement.

The Mayo Foundation has now embarked upon the praiseworthy goal of establishment of a medical school. It too will undoubtedly become a quality operation of great distinction. It will be interesting to observe over future decades whether the School or the Clinic will become the dominant force in determining the directional trend of the Mayo operation. Despite his predominantly practical turn of mind, Dr. Judd had a keen interest in research and in organizational medicine and its continual uplift. I believe, therefore, that he too would have welcomed and supported this new alignment of objectives within the Mayo Foundation and Clinic.

Fortunate indeed is the medical school or clinic that has within its staff a surgeon with the skill, judgment and stature of Dr. Judd, possessed too of an unusually fine and perceptive appreciation of the importance of research for surgery's advance and progress.

Owen H. Wangensteen, M.D.
Regents' Professor
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University of Minnesota

Gonorrhea at a Teenage Medical Service

MINNESOTA HAS FOR more than 55 years been proud of its record in venereal disease control, beginning with a World War I VD Control Program initiated by Dr. Harry G. Irvine, a long-time Minneapolis dermatologist and consultant for the Minnesota Department of Health. Changes in the clinical situation have been dramatic as illustrated by Jerome et al.* They describe a study of VD detection in the Teenage Medical Service of Minneapolis, indicating changes in sexual behavior especially among younger persons. Nevertheless, it is encouraging that data, from other sources, confirm Minnesota's relatively favorable status with regard to VD control.

The authors describe a one-year study covering 6085 patients from 13 to 20 years of age. Results of their study confirm the diagnostic need for use of both smears and cultures. In female patients the cultures were much more reliable and lack of culture often results in failure to establish the correct diagnosis. The smears can be difficult to evaluate. Generally there has been acceptance of a view that in males the results of smears and cultures will be in agreement. The authors found disagreement in 17% of their male patients and therefore emphasize the need to use both techniques. A report of the results of serologic tests for syphilis in the patients with gonorrhea and in all patients included in the study would have been an interesting addition to the publication. (Perhaps the authors can easily provide this information as an addendum.)

A striking commentary on the need for concern about VD in teenagers is the authors' reference to the need for re-study with "each change of sex partner or when doubts of the partner's fidelity arise". For many of us it is still easy to recall the days when patients with venereal diseases were regarded by many physicians and the majority of lay persons with more scorn than pity.

Francis W. Lynch, M.D.
St. Paul, Minnesota

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*See page 245.

Medical vs. Economic Progress for Diabetics

DIABETICS HAVE long suffered unwarranted discrimination when seeking employment. The Federal government would not employ known diabetics in any capacity prior to 1941. Until 1969, Hennepin County had no classes of jobs open to diabetics. Although a recent survey study shows that most companies replying to a questionnaire have favorable employment policies for diabetics, only a minority of the companies replied.[1] The respondents probably represent the more liberal employers.

Experiences of the Twin Cities Diabetes Association Employment Committee suggest that despite the variability of job demands and the obvious differences in severity and control of the disease, many employers unfortunately still hesitate to hire a qualified diabetic for a job he can perform well. Such blanket rejection policies fail to consider the last fifty years of progress in diabetes management and the performance data accumulated from companies employing large numbers of diabetics. Ironically, the same employers rarely dismiss employees who become diabetic after employment, presumably because job performance is satisfactory.

At least 2%, and possibly 4% of the United States population are diabetic. In the majority the diabetic state is controllable by diet alone or diet and an oral hypoglycemic agent. Only 10% or less require insulin therapy. The severity of the diabetes is variable both in terms of metabolic control and associated complications such as retinopathy, neuropathy, nephropathy, and vascular disease.

Jobs vary too. Some are hazardous to anyone, but especially hazardous to a person who might lose consciousness—a remote, but definite possibility in the insulin-taking diabetic. Other jobs involve large expenditures of energy in unpredictable short periods of time. Still others require changing hours or split-shifts. Such jobs may complicate control in the insulin dependent diabetic, but with proper management, can be handled by the majority. A great number of jobs are sedentary and should be open to virtually all diabetics.

Employers' objections to the hiring of diabetics center basically around four concerns: (1) Concern that excess absenteeism will result in poor job performance; (2) Concern that on-the-job insulin reactions will result in job disruption or injury; (3) Fear that excess responsibility for injuries or disability due to injuries will result from the diabetic state; and (4) Fear that adverse effect on group medical insurance rates will occur. Such objections may be valid in a few diabetics but most diabetics can perform well in jobs for which they are otherwise qualified.

Though the data available is sparse, more than two-thirds of replying employers in one large survey reported average to superior absentee records in their diabetic employees.[2] In a very carefully followed group, a large utility company over an eighteen year period noted absenteeism among diabetic employees to be 33% less than among non-diabetics.[3] Weaver and Perret, in a study of diabetics employed by a large oil refinery and petrochemical plant, found no significant increase in sickness absenteeism and no impairment of work effectiveness in their diabetic employees, although some require special job placement.[4] Pell and D'Alonzo found a less favorable record among DuPont employees, and stressed the need to assess risk on an individual basis.[5] Nasr, et. al., at Ford Company, found that diabetics tended to be absent more frequently and for longer periods of time, but in the year studied, 73.5% of their diabetic employees had no reportable absences whatever.[5] This variability noted in attendance and performance might well be related to differences in severity of the disease and appropriateness of job placement.

Little or no data is available to deal with the question of on-the-job insulin reactions. It should be noted though that the liberalization of driver laws for diabetics in Minnesota has not led to an increase in accidents due to insulin reactions. Insulin reactions, unlike other changes in consciousness such as seizures, are predictable, usually preventable, and with rare exceptions, begin with mild warning signs, which the diabetic can recognize and correct by ingestion of carbohydrate. Most diabetics never have reactions, and those who do can be trained to recognize them early and abort them before they become serious.

Fear of excess financial loss for on-the-job injuries is unwarranted if diabetics are carefully matched to jobs they can perform. Although diabetics may develop complications from injuries more readily than non-diabetics, in most states including Minnesota, second injury laws are available to protect the employer against excess loss due to complications from the pre-existing diabetes, and against all losses from injuries directly related to the diabetes provided the diabetic employee is registered with the state.[7]

The question of increased rates for group medical insurance is a complex one. Such rates are based on the quality of coverage and cost-experience of the group. One can only point out that many medical conditions and other factors affect the risk of any given group. Most companies do not hesitate to hire an employee with a diabetic spouse or child who becomes part of the same insurance group and affects the group's rate to the same extent as the diabetic employee.

Diabetics have the same desires for personal productivity and financial independence as others. Much progress has occurred in medical management since the discovery of insulin fifty years ago, and the great majority of diabetics can now perform well in most jobs. Because of insulin dependence and/or complications, some diabetics cannot perform some jobs, and a few are unemployable. If both personal and personnel physicians apply the screening procedures suggested by Cohen and Mastbaum,[8]* these latter groups are readily identifiable, and can be selectively rejected for jobs to which they are unsuited without penalizing the well controlled majority. Medical progress in diabetes has been reflected in liberalized government employment policies, driving laws, insurance benefits, and should now be reflected in liberalized employment policies in the rest of our economy. The diabetic seeking employment is an individual applying for a specific job. The diagnosis per se is no longer adequate grounds for rejection.

Leonard Mastbaum, M.D.
Minneapolis, Minnesota

References 1-8 will be found on page 226.

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*See page 241.

Management of Pain with Nerve Blocks

In the management of man's painful afflictions, local anesthetic infiltration and nerve block techniques play a decided role. The precise role depends on the cause and location of the pain. The intrathecal injection of minute amounts of Phenol for painful perineal carcinomas rivals in effectiveness—though not in risk—the stellate ganglion block for the patient with a post-traumatic sympathetic dystrophy. On the other hand, injection therapy with or without accompanying physical therapy has seldom been of value in chronic cervical sprains ("whiplash").

The importance of the graded isobaric spinal block, not often enough performed because of its complexity, needs emphasis. "Central" pain, that is pain independent of a peripheral stimulus, does exist. Once one sees a patient totally anesthetic below the nipple line, unable to move or to feel a severe noxious stimulus in the foot and yet persisting in complaints of foot pain, one realizes that "central" pain is something beyond our present understanding and certainly not amenable to cordotomy or rhizotomy.

Dr. Black* in his paper emphasizes proper techniques and dangers. When he states that the most frequent complication of nerve block is simple overdosage he chides us all. That certainly should be avoidable. A proper armamentarium is important to adequately deal with the infrequent but potentially catastrophic complications of local anesthetic injections.

Finally, a word of caution is needed. Chronic benign pain is a therapeutic dilemma of major proportions. Our enthusiasm for treatments leads us to diagnostic local anesthetic blocks. This enthusiasm must be tempered with caution if not with scepticism. The extrapolation that one makes in sectioning the fifth lumbar root following a successful block of that root contains two faulty assumptions: first, it assumes that the anesthetic agent is the only factor working on the patient at the time of the block; second, it assumes that the permanent effects of surgical section of that root equal the six-hour effects of the nerve block. We have all seen the ability of the nervous system to recover at least in part from injury, and this includes carefully designed surgical injury.

John L Seymour, M.D.
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*See page 189.

Acupuncture Analgesia

Analgesic effect of acupuncture has been observed by Chinese physicians for centuries. That acupuncture restores the interrupted flow of energy and thus relieves pain has been a prevailing theory to interpret this phenomenon.

Recently, investigators in China have shown that in rats and rabbits, acupuncture has a definite inhibitory effect on the pain response recorded in the thalamus and the mid-brain reticular formation. They have demonstrated that acupuncture raises the pain threshold significantly in human volunteers. If a nerve block was first performed, however, acupuncture failed to change the pain threshold. They thus conclude that acupuncture has more than a suggestive or placebo effect, speculating that spinal cord, medulla, mid-brain reticular formation, thalamus and cerebral cortex may play some integral role in the analgesic effect of this modality.

The criteria for acupuncture analgesia include:

1. The sensory pathway conducting acupuncture stimulation to the central nervous system must be intact.
2. Sufficient stimulation, manual or electrical, must be applied.
3. Induction period of 20 minutes or more may be necessary for the analgesic effect to reach a peak.
4. Analgesic effect may be incomplete.
5. Different combinations of loci selected for stimulation often achieve the same analgesic effect.

It is apparent that inconsistency exists in an effort to obtain acupuncture analgesia. Multiple factors may be involved in this phenomenon.

Dr. Melzack's* excellent article in this issue indicates that psychological factors and his revised

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*See page 161.

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gate-control mechanism may be the acceptable theory for a better interpretation of acupuncture analgesia. At last, a physiological factor is being recognized as part of its mechanism.

While this theory is very logical and attractive, it is premature to discard entirely the meridian theory without further scrutinization. Furthermore, it is tempting to speculate that some unknown chemical analgesic may be released at some level of the central nervous system following the mechanical stimulation of the peripheral nerves.

Josef K. Wang., M.D.
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Management of Chronic Disabling Pain

PAIN IS A UNIVERSAL experience, invaluable as an alerting and protective device in maintaining health. The physiologic basis for pain production, transmission, and appreciation remains unknown despite careful study and the construction of elaborate theories. The phenomenon is purely subjective. The physician's awareness of its presence and its characteristics depends almost entirely upon the patient's ability to observe and report accurately. No satisfactory method exists for assessing pain objectively. Managing pain requires accurate diagnosis and correction of the underlying causative lesion, if possible.

If specific treatment for the underlying disorder is unavailable, or if the nervous system is permanently deranged despite the removal of the disorder, a disabling chronic pain may supervene that defies all attempts at pain control. In this difficult and frustrating setting, new and innovative treatments may be used in an attempt to obtain relief. When such procedures are considered, it is mandatory to have the clearest possible understanding of each patient's disease, and to study the results of treatment with the utmost care. Subjective, emotional, and psychologic distortions of the results of such efforts by the patient or his physician can lead to false impressions and undue hope or pessimism.

Transcutaneous stimulation, an electronic form of counter-irritation, has become available for the management of chronic disabling pains in the past several years. Developed on the basis of the "gate theory" (itself unproven) of pain modulation and appreciation, this technique has been shown to help some patients by all physicians who have used it. As might have been expected, however, it has not solved all such problems.

Elsewhere in this issue,* another report points out that the transcutaneous stimulation helps some patients with chronic pain. The report also demonstrates some of the problems inherent in attempts to study and to correct such problems. The author's stated intention was to describe his experience in treating 400 patients with chronic intractable pain, using transcutaneous stimulation. It actually reports on only 197 patients; 203 were excluded because "they failed to complete the protocol" (53 patients), or because they were apparently participating only in the initial phase characterized by the investigators as learning to use the technique (150 patients).

The "disease states treated" are listed in Table 1 (for the initial phase of study and treatment of the 197 patients). Table 2 refers to the same patients, followed for one year and studied by responses to a mailed questionnaire. The diagnoses listed in the two tables are surprisingly incongruous. Chronic prostatitis, carpal tunnel syndrome, pancreatitis, brachial plexus injury, and headache appear in Table 2 for the first time, while lumbar osteoarthritis, cervical osteoarthritis, peripheral neuropathy, and postherpetic neuralgia are not carried over from Table 1. The reason for these changes in diagnosis is not clear. The largest category of patients treated was that of "chronic low back pain with arachnoiditis" (Table 1), and "chronic low back syndrome" (Table 2). (Did the arachnoiditis subside during the interval?) Arachnoiditis is often invoked as a cause of chronic back pain after multiple surgical procedures upon the lumbar spine, though the accuracy of this diagnosis and the criteria for making it are sometimes uncertain. All patients probably have some degree of scarring after multiple surgical procedures upon the lumbar spine and related structures, though most patients do not have problems with severe postoperative pain. Because this was the largest group of patients treated, the author probably should have presented his criteria to determine the presence of arachnoiditis extensive enough to cause severe and obstinate pain.

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*See page 195.

New techniques of treatment require careful study to determine their ultimate usefulness and safety. Transcutaneous stimulation is a harmless procedure, beneficial for managing intractable pain in some patients. However, honest efforts to control chronic pain syndromes require difficult and time-consuming assessments of a subjective, emotion-laden phenomenon. This fact makes a careful scientific approach all the more necessary, before the profession can accept the results and conclusions.

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Letter to the Editor

Dear Editor:

The article by J. F. Berlauk's* presents a concise review of the data supporting the efficacy of Rh Immune Globulin in preventing erythroblastosis fetalis. It emphasizes the importance of treating all women meeting appropriate criteria. It fails to point out that such treatment should also be given to unsensitized Rh negative women following an abortion.

The article also states that RhIgG is not suggested for the treatment of an Rh negative patient transfused with Rh positive blood by mistake and further studies are needed. In fact at least one manufacturer of RhIgG, Ortho (RhoGam^{TM}), now states in their product brochure, "RhoGam^{TM} is used to prevent the formation of active antibodies in the $Rh_o(D)$ negative, D^u negative individual who has received Rh positive blood as a result of delivering an $Rh_o(D)$ positive or D^u positive infant, *or as a result of a transfusion accident.*"

One of us (HFP) has directed the treatment of three such cases with apparent prevention of sensitization. We recommend that treatment of a transfusion accident should be restricted to well hydrated female patients who are *not,* but might become, pregnant. The dose of RhIgG must be carefully calculated to insure administration of an adequate volume to cover the amount of Rh positive blood given.

Herbert F. Polesky, M.D.*
Edward L. Segal, M.D.†
Minneapolis, Minnesota

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*57:47, 1974.
*Minneapolis War Memorial Blood Bank.
†Methodist Hospital

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Medical vs. Economic Progress for Diabetics—Mastbaum (page 222)

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Scan Conference

G.I. Bleeding in A Six-Month-Old Girl

A SIX-MONTH-OLD baby girl was well until the day of hospitalization, when the mother noted dark red blood in the stool. The past history and physical examination were negative. The Hgb was 8.7 gm.%. A barium enema examination done on the same day disclosed a normal colon with no evidence of intussusception. On the next day the patient was given Tc^{99m} sodium pertechnetate, 3 mCi, intravenously and the abdomen was imaged by means of a gamma (Anger) camera (Figure 1).

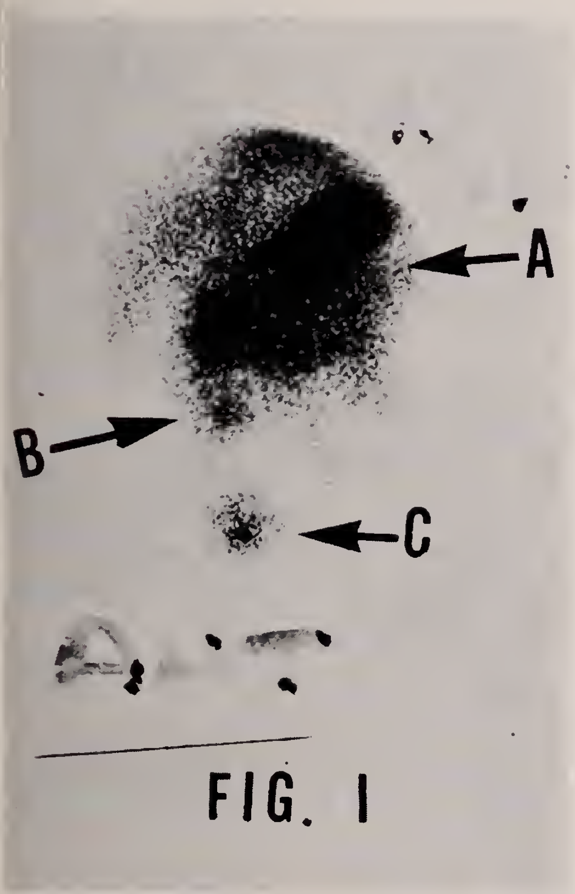

Fig. 1—Scintiphotogram 15 minutes after injection of Tc^{99m}. A—Stomach and proximal small bowel. B—Meckel's diverticulum. C—Urinary bladder.

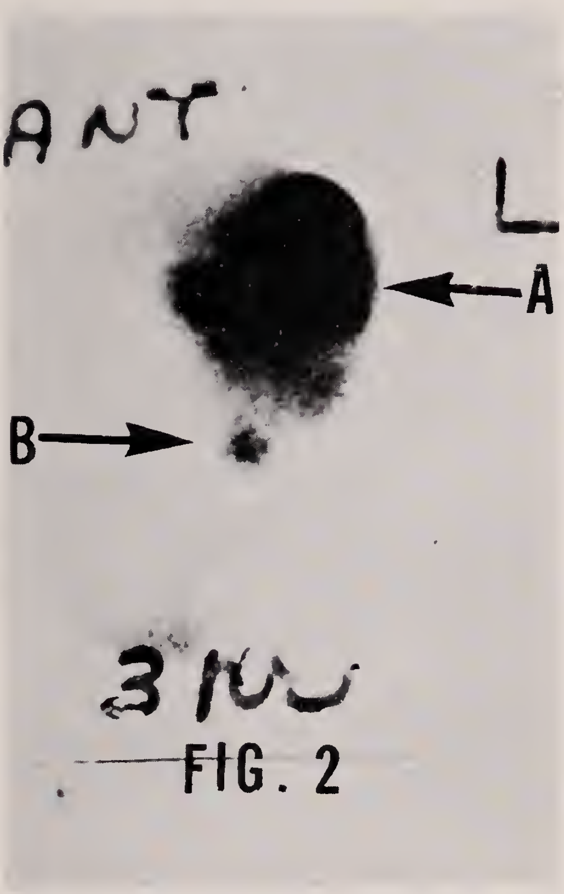

Fig. 2—Three-hour image. A—Stomach and proximal small bowel B—Meckel's diverticulum.

Diagnosis: Bleeding from Meckel's diverticulum.

At 15 minutes following injection of the radionuclide the scintiphotogram demonstrates cencentration of radioactivity in the stomach, proximal small bowel, and bladder (Fig. 1). In addition there is a circumscribed round area of radioactivity inferior to the proximal small bowel, consistent with a Meckel's diverticulum. At three hours (Fig. 2) both the diverticulum and the stomach show further increase in radioactivity. The bladder has been emptied.

Technetium 99m is excreted by the gastric mucosa, and its gamma emissions are thus concentrated in the stomach. Among those Meckel's diverticula that contain heterotopic gastric mucosa about a half will show simultaneous concentration of radioactivity on the scintiphotogram, as illustrated in this case.

Approximately 55% of Meckel's diverticula have heterotopic gastric mucosa and are a recognized source of gastrointestinal hemorrhage in infancy. The bleeding is caused by peptic ulceration, usually of the adjacent ileal mucosa, and may be massive. Visualization of the Meckel's diverticulum by roentgenologic methods (g.i. series, barium enema), unfortunately, is seldom successful. The radioisotope method using Tc^{99m} is a valuable diagnostic aid but not without its limitations. In addition to a 50% incidence of false negative results, false positive results have been reported in a variety of conditions such as intestinal obstruction with or without intussusception, ingestion of irritating medication, hemangioma, aneurysm, intestinal ulcer, partial ureteral obstruction, retained feces in cecum, etc. Repeated scanning, both early and late (Figures 1, 2) may help to avoid some of these pitfalls.

In this case a subsequent g.i. series indeed failed to demonstrate the Meckel's diverticulum or any other cause of hemorrhage. The patient had surgery on the 8th day of hospitalization because of falling hemoglobin values. A Meckel's diverticulum with gastric mucosa was found and excised. There has been no recurrence of bleeding or anemia since the operation.

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Book Reviews

LEUKEMIA IN CHILDHOOD. André D. Lascari, M.D., Professor of Pediatrics, Southern Illinois University, School of Medicine, Springfield, Illinois. Charles C. Thomas, Springfield, 1973, pp. 486. $16.75.

The author has made a thorough and comprehensive survey of the English literature pertaining to the incidence, etiology, epidemiology, and pathophysiology of all types of leukemia in childhood.

Clinical criteria, manifestations, laboratory findings, morphological aspects, therapy, prognosis, and complications are presented. The pharmacology of antileukemic drugs, their therapeutic effectiveness, metabolism, toxicity are critically evaluated.

Chromosome abnormality in myeloid cells, erythroblasts, and megakaryocytes as an aid in diagnosis is discussed. Clinical examples of preleukemia are presented. The author defines the preleukemia phase as "the present of hematological abnormalities without bone marrow or tissue evidence of leukemia which, after a variable time evolves into leukemia." In the chapter "Unusual Forms of Leukemia" Lascari takes up conditions such as congenital leukemia, erythroleukemia, eosinophilic leukemia, basophilic leukemia, myelomonocytic leukemia, and others.

An unique innovation is the chapter "Emotional Aspects" in which Dr. Lascari emphasizes the emotional aspects of the patient, parents, and the fact that the physician has an emotional investment not only to the patient but also to his family.

Some of the black and white photomicrographs are of poor quality making it difficult to appreciate morphological detail. The color reproduction of leukemic cells with the exception of Plate 4 lack the tinctorial range of Wright's stain.

The binding, layout, and type reflect fine workmanship. The book is extensively referenced and well indexed. I am inclined to concur with Dr. Donald Pinkel who in the Foreword states: "For the teacher and practitioner it is the most authoritative current source of knowledge about leukemia."

Emil Maro Schleicher, Ph.D.
Minneapolis, Minnesota

THE PRINCIPLES OF CLINICAL ELECTROCARDIOGRAPHY. Mervin J. Goldman, Lane Publishing Company. $8.00. 400 pages.

The eighth edition of Goldman's book, *The Principles of Clinical Electrocardiography,* remains the best introductory book on the clinical approach to electrocardiography. This book is not, nor does it intend to be, an indepth study of electrocardiography; rather it presents a comprehensive and straight forward approach to the basic understanding and clinical application of this valuable diagnostic tool. Dr. Goldman begins with the most elementary aspects of electrophysiology of the heart and develops from this the normal and abnormal electrocardiographic configurations and cardiac vectors. Included in this elementary book are chapters on the more recent sophisticated aspects of electrocardiography such as His bundle recordings and the concept of fascicular blocks. The chapter on spatial vectorcardiography provides a brief, comprehensible introduction to vectorcardiography.

The book lacks sufficient detail and depth to be of great interest to the internist or cardiologist but deserves to be placed first among the introductory books on the approach to clinical electrocardiography.

Robert Van Tassel, M.D
Minneapolis, Minnesota

CONFERENCE ON IMMUNOLOGY OF CARCINOGENESIS: National Cancer Institute Monograph #35, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402 @ $9.75, stock number 1742-004.

A report from the Conference on Immunology of Carcinogenesis, held by the Oak Ridge National Laboratory at Gatlinburg, Tennessee, May 8-11, 1972. Participants were invited to discuss possible means of using tumor specific antigens as a basis for studying the etiology, diagnosis, prevention, treatment, and prognosis of cancer. Papers presented are related to: (1) What can immunology do for the prospective cancer patient from the point of view of detection and diagnosis? (2) What therapy can immunology provide for the patient with an established tumor or with widely disseminated tumor? (3) Against what type of tumors and under what conditions can immunotherapy be directly applied with demonstrable beneficial effects?

The answers to the questions posed by the Conference are less than complete. The reader, however, will be able to obtain a picture of the problems of tumor immunity and where the field is heading. Unfortunately, no safe and effective anticancer vaccines presently exist for human use and the availability in the near future appears unlikely. A major impetus to the session was the demonstrated successful immunotherapy of human skin cancers with long term cures.

Most of those with interest or specialized knowledge in this field would appear to have been either participants in the sessions or guests at the Conference.

Victor A. Gilbertsen, M.D.
Minneapolis, Minnesota

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E. Starr Judd, M.D.
Eminent Mayo Clinic Surgeon
1878-1935

WALTMAN WALTERS, M.D., M.S. IN SURGERY, SC.D. (HON.)*

Dr. E. Starr Judd recognized by surgeons all over the world as one of the greatest of his time.

EARLY IN THE HISTORY of the Mayo Clinic, the fame of the Mayo brothers—William J. Mayo and Charles H. Mayo—had spread far and wide in this country and abroad. Surgeons came to Rochester from all over the world to see "Dr. Will" and "Dr. Charlie" operate, and to hear them discuss their cases. It was soon apparent to the visitors, however, that there were other fine surgeons, trained by the Mayos, working in the hospitals associated with the Mayo Clinic who could operate rapidly and skillfully on patients with surgical lesions located almost anywhere in the body. Among these was E. Starr Judd, a man who was, in the opinion not only of the medical and surgical community of the Mayo Clinic but also of the surgeons of the United States and other countries, one of the greatest surgeons of his time.

Biographic Outline

E. Starr Judd was born in Rochester, Minnesota, on July 11, 1878. His parents were both descendants of the pioneer Connecticut families of Judd, Meyers, and Starr. Starr's father, Edward Francis Judd, had migrated to Rochester because of his health. Dr. Comfort Starr, one of the founders of Harvard College and a practicing physician, was one of Starr Judd's forebearers. Starr Judd attended public schools in Rochester and was graduated from the University of Minnesota Medical School (Figures 1 and 2) in 1902. He then interned at St. Marys Hospital in Rochester and later served for a year as Dr. Charles H. Mayo's first assistant. Following this he was appointed to the staff of the Mayo Clinic.

In 1908 Starr Judd married Helen Berkman, one of the three daughters of the Mayo brothers' sister, Gertrude Mayo Berkman. The Judds had

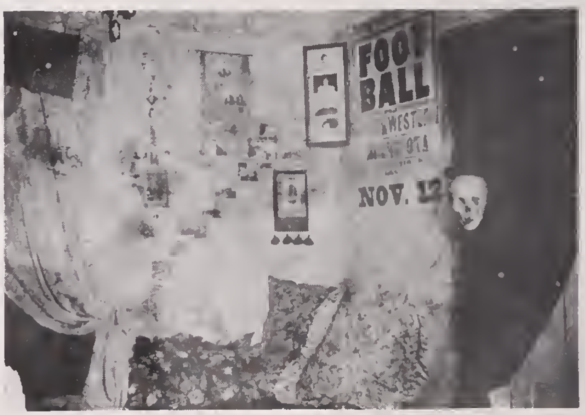

Fig. 1—E. Starr Judd's room at the University of Minnesota Medical School.

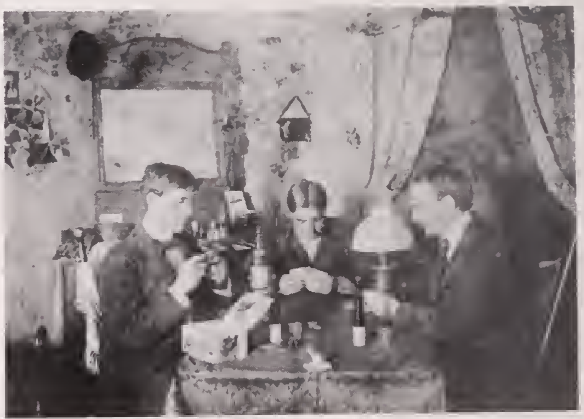

Fig. 2—E. Starr Judd *(right)* in a recreational game of chance while a student at the University of Minnesota. One of the players was Henry McQuigan of Red Wing.

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*Emeritus Member, Department of Surgery, Mayo Clinic and Mayo Foundation; Emeritus Professor of Surgery, Mayo Graduate School of Medicine (University of Minnesota); Rochester, Minnesota.

Presented before the Mayo Foundation History of Medicine Society on July 11, 1973 (birth date of E. Starr Judd, M.D.).

See editorial, page 219.

ive children:* Edward S. Judd, a surgeon of the Mayo Clinic, who has made many contributions o surgery and has been rewarded by election to amous American invitation surgical societies and o the presidency of the Central Surgical Association; David, a surgeon in Eugene, Oregon; Eleanor Judd Kirklin, a realtor of Rochester; and Mrs. Mathew (Mary Jane) Patton, the wife of a pathologist of Eugene, Oregon. Like their mother and father, all have become leaders in their communities. His brother, Neil, was a Rochester pharmacist.

In 1919 Starr Judd became Professor of Surgery in the University of Minnesota's affiliated Mayo Graduate School of Medicine and Chief of the surgical staff of the Mayo Clinic. By then he was well known as a surgeon of vast experience with excellent clinical results. He was sought after as a speaker at all types of medical and surgical meetings, including those of the American and the Minnesota Medical Associations, the American College of Surgeons, and the most prestigious of the invitation surgical societies such as the Society of Clinical Surgery and the American, Western, and Southern Surgical Associations. In all of these organizations, he was elected early in his career to membership; later he was elected President of the Minnesota State Medical Association (1923), the American Medical Association (1931) (Figure 3), the Western Surgical Association (1929), and the Society of Clinical Surgery (1932). He was immensely well liked and had many close friends among their members. He was particularly fond of the members and the meetings of the Southern Surgical Association, an association that, at that time, had elected few surgeons from the North to its membership. In 1934 he received the honorary degree of Doctor of Science from the University of Maryland.

Membership in professional associations was important to Starr Judd; ironically, it was while he was on his way to a surgical meeting in the East that he became ill from a virulent pneumonia. E. Starr Judd died on Nov. 30, 1935, at the Presbyterian Hospital in Chicago.

Dr. Judd As a Surgeon

Starr Judd had the largest surgical service in the Mayo Clinic, and was a prodigious worker, student, and teacher of surgery. In 1921, when I was his second assistant, he had from 100 to 105 surgical patients on his service at St. Marys Hospital. Clinically, his results were excellent and he had a very low mortality rate, even in the most complicated cases. He not only enjoyed but really loved being a general surgeon, and particularly enjoyed biliary, gastrointestinal, and urologic surgery. Starr Judd was a general surgeon in the sense that his work embraced not only diversified operative surgery but also clinical investigation, research, and teaching. The scope of Starr Judd's work is illustrated by his bibliography; for the period 1908 through 1936, his bibliography listed 339 publications. His contributions included papers on surgery of the head and neck (some of which dealt with surgery of adenomatous and exophthalmic goiter and of the larynx), fractures, and surgery of the urologic, gastrointestinal, and biliary tracts. Up to the end of 1921, when I became one of his second assistants, he had published 86 papers.

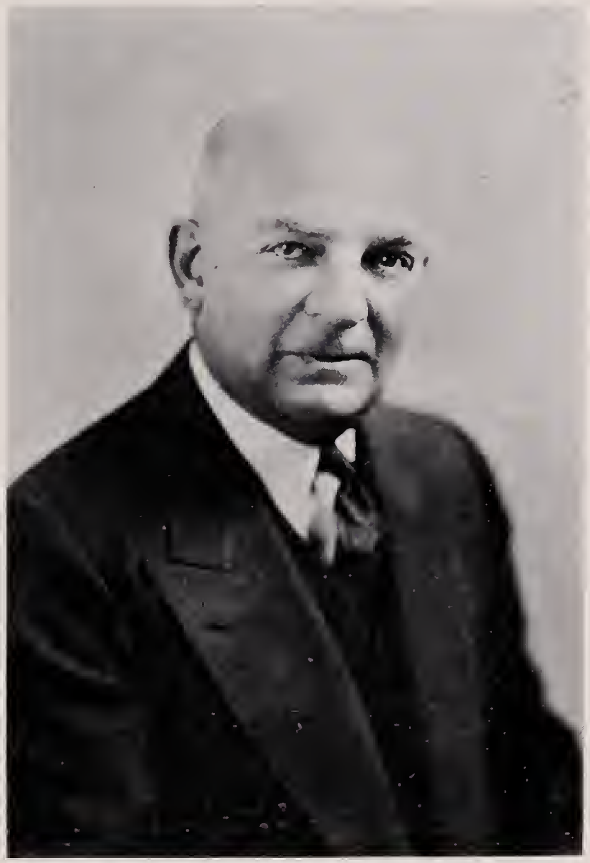

Fig. 3—E. Starr Judd, when he was President of the AMA (1931).

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*One daughter, Mrs. Thomas B. (Helen Phoebe) Tooke, passed away on Aug. 7, 1972.

Surgical operations were scheduled six days a week at St. Marys and the Colonial hospitals, and emergency operations were done when necessary. Dr. Judd operated on five mornings a week. He arrived at St. Marys Hospital at 7:15 A.M. After making complete surgical rounds with his second assistants, he and his surgical team began operating at 8:00 A.M., continuing until he finished his long operative list. As a surgeon, one of his outstanding qualities was an ability to make immediate decisions during the operation about the proper operation to be performed on each patient after considering the risk of comparative operations and their respective end results. Assisted by his team of skillful assistants, his anesthetist, and his operating room nurses, his work rarely could be equalled by others. Then, and since then, I have seen few surgeons working with their surgical teams who could duplicate it.

His first assistant was Fred Rankin, who became a member of the Mayo surgical staff in 1926, and later distinguished himself as a surgeon in Lexington, Kentucky. Sister Mary William (Sister "Bill"), like Dr. Judd, was a sports enthusiast, and developed a reputation as such among the Mayo surgical group and Fellows. She became known and was a favorite of many amateur and professional athletes; members of the Notre Dame football team sent her a football used in one of their games which they had individually autographed. His anesthetist was Miss Serena Huntimer, a sister-in-law of Mayo gastroenterologist Dr. George B. Eusterman.

Dr. Judd operated exclusively at St. Marys Hospital, as did Dr. Will and Dr. Charlie. All of the surgical fellows at St. Marys Hospital working with other surgeons sought opportunities to assist Dr. Judd when the surgeons they had been assisting had finished their surgical schedules. The additional operating room was quickly prepared for the use of other surgeons because Dr. Will and Dr. Charlie had two operating rooms to use (each operating on alternate days) while the other surgeons had only one. These surgeons' assistants would come into Dr. Judd's operating room and ask if they could put his next patient on the operating table in their room for him. Thus, with two groups of assistants opening and closing the operative incision, he was able to do twice the number of operations in almost the same time as if he had only one group.

His afternoons were occupied by his consulting practice at the Mayo Clinic. He met with hi second assistants each afternoon in his clini office and reviewed with them the histories c the patients to be operated upon the followin day. His first assistant had been with him during his consultations. At these meetings, for eac patient, the history, symptoms, results of laboratory studies, and indications for the surgical procedure were discussed. This was of great valu to the assistants and the patients, and to Dr Judd too, for this review helped him to decid whether further laboratory studies should b made or whether the patient should be prepare further before the operation. This particularl applied to patients in whom jaundice and othe liver dysfunctions complicated biliary lesions, an in whom dehydration had occurred not only from obstructive lesions of the biliary tract and of th upper gastrointestinal tract in cases of pepti ulcer or gastric ulcer but also from disturbe renal function in cases of urinary tract obstructions.

In order to give his assistants a chance to participate in clinical and surgical studies that interested him, he frequently asked one of hi assistants to join with him in the study and t write the first draft of the report of these studies thus there were many coauthors of his publishe papers. After discussion of a paper with a coauthor, he might change or rewrite and edit i before sending it to the Mayo Clinic Editoria Section for final editing. His interest in surgica education by the written word, I believe, was the reason for his acceptance of and appointment t the post of Associate Editor of the *Archives o Surgery* and of the *Lewis' Practice of Surgery*. A similar appointment to the *Annals of Surgery* is now held by his son, Edward Judd.

He was as interested in his assistants as he was in the welfare of his patients. His daughter, Mrs. Eleanor Kirklin, told me that only later in his lifetime did she find out that her father had become famous as a surgeon and had provided financial support to many young men who would not otherwise have been able to afford to atten medical school. Practically all of his assistants became famous or well-known surgeons, including many appointed to the permanent staff of the Mayo Clinic; and many of the surgical Fellows (Residents) were appointed to the teaching staffs of University Medical Schools and their affiliated hospitals in this and other countries.

here they became professors of surgery.

One morning each week, he took his assistants nd some of the visiting surgeons to the Experi- iental Institute, where they visited the labora- ories of Frank Mann and his associates Jesse ollman, Tom Magath, Hiram Essex, and George iggins; William Feldman and Carl Schlotthauer both D.V.M.'s), who were studying diseases and umors of animals, also were associates. All of iese doctors became famous in their specialties. hey all discussed their experimental studies, specially those which had important application o patient's surgical problems. Most frequently hese problems were related to the biliary and astrointestinal tract; later, the results of Dr. udd's investigative surgical studies frequently vere presented to meetings of national medical ind surgical societies.

Dr. Judd As a Colleague

As a person, Starr Judd was modest, generous, ind kind to everyone. Although a little shy, he vas a fine companion, had a delightful sense of iumor, and was fun to be with. He was equally it home with participating graduate students (Fellows) in the Mayo Foundation, visiting surgeons observing him at work in his operating room (Figure 4), and colleagues attending scientific meetings where he was a speaker. He had many interests outside of surgery and some of these are best illustrated by anecdotes.

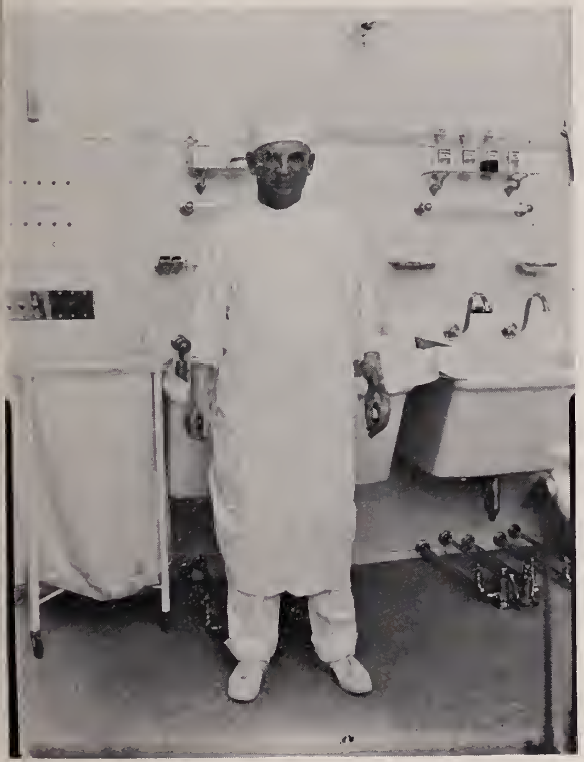


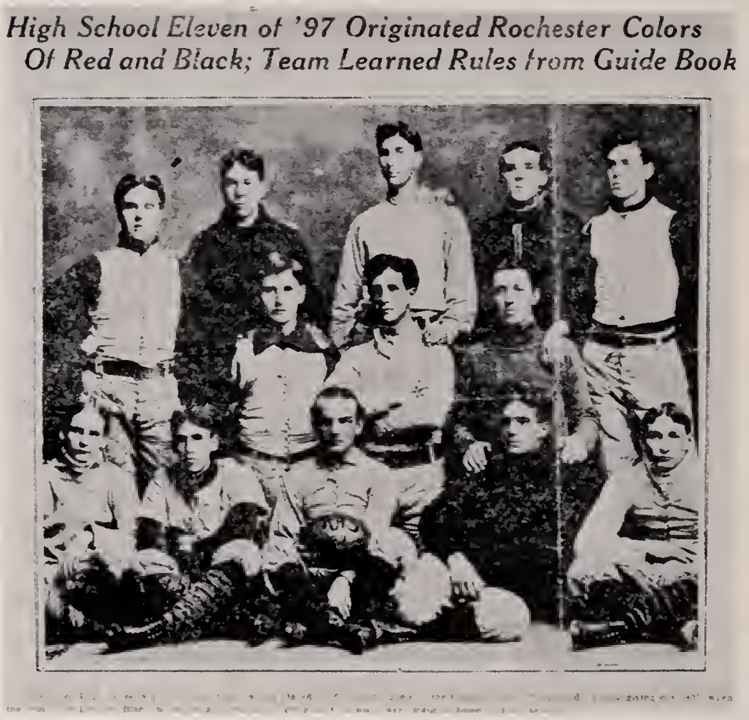
Fig. 4—E. Starr Judd in his St. Marys Hospital operating room.

In whatever he did, however, he was never far from surgery. For example, he enjoyed going on picnics with members of the Mayo and Berkman families and their friends and was always careful to protect his hands. Mrs. Henry Plummer has told that the only help he would give at these picnics was to fold the napkins.

He had a lifetime interest in cardplaying, particularly poker, and also in all sports. He was team captain in the first football game ever played in Rochester (Figure 5), and his continuing interest in football led him to donate anonymously the field house in Soldiers Field to the city of Rochester to provide a place for the football and baseball players to change their clothes and to shower. The pool was built later. It was typical of Starr Judd that he did not voice this abroad, and Mrs. Kirklin, his daughter, said that her father never told the family of this or other of his gifts.

Because of his interest in all sports, he received many invitations to attend football and baseball games, and boxing events and championship prize fights in Chicago, Philadelphia, New York, and Minneapolis; these invitations were from grateful patients on whom he had operated and also from surgical colleagues in other cities, some of whom he had also operated on.

His interest in athletic sports and activities continued throughout his life. He was, for example, a good golfer. He promoted tournaments between golfers of the Rochester Golf and Country Club and Minneapolis and St. Paul doctors at their respective clubs. He and his brother-in-law, Dr. Henry Plummer, and Dr. Balfour, who had bought land in the rolling hills about eight miles west of the Mayo Clinic between Rochester and Byron, thought that a nine-hole golf course and a club house could be built on it, so they donated it to form a club. The club became so popular among staff members (and Fellows, whose dues were low and paid in part by the Mayo Foundation) that some years later it was enlarged to become a beautiful 18-hole course. Today, the trees that were planted then have attained their full growth and the golf course is considered to be one of the most attractive and



High School Eleven of '97 Originated Rochester Colors Of Red and Black; Team Learned Rules from Guide Book

Fig. 5—1897 Rochester High School football team. E. Starr Judd (holding ball) was team captain.

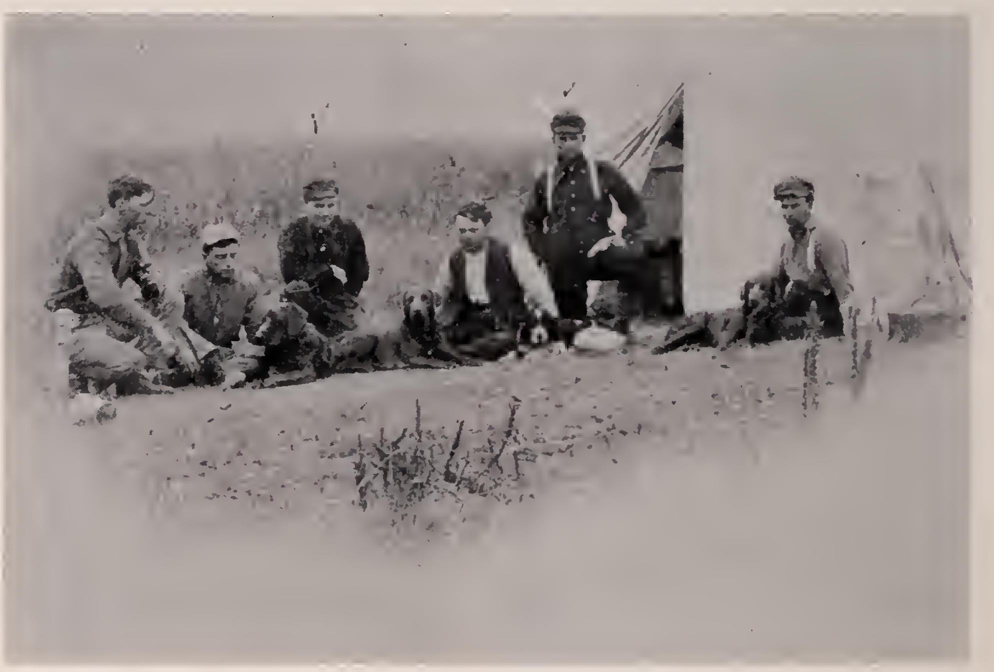


Fig. 6—E. Starr Judd *(third from left)* with Mr. Harry Harwick *(extreme left)* and Dr. David M. Berkman *(second from left)* with others on prairie chicken hunting trip at Hallock, Minnesota.

autiful of any of our American courses of nilar length. The only thing it lacks is a water le.

Dr. Judd greatly enjoyed hunting, particularly ith his brothers-in-law and close friends in-uding Harry Harwick, Harold ("Pete") Lillie, d Harry ("Hasty") Wood (Figure 6). Some of s hunting trips were in contrast to the surgery acticed in Rochester. One such trip was so entful that its memory remains fresh. This as a noteworthy hunt I took part in with Drs. dd, Plummer, and David Berkman. It was a alking nightmare across frozen bays and through rests without trails to reach moose hunting ter-tory in Ontario in mid-November in 1922. We ere to meet a hunting guide on the Minnesota hore of Crane Lake, one of the Minnesota bor-er lakes. Because of the early freeze it was not ossible to use a houseboat. All of us had can-eled our schedules so we decided we would walk o the hunting area—a rugged trip for all of us. The first day we walked an almost unbelievable 2 miles from the Minnesota shore of Crane Lake o a loggers' camp, where we had an excellent ot meal. Dr. Judd, who had operated on the oreman, was invited to stay with the foreman in is cabin; the rest of us spent the night in a huge single-room cabin in company with 30 or 40 oggers, who slept in rows of upper and lower iron bunks. It was cold, and so there was a hot log fire in a large stove in the middle of the long, single room. None of us had ever experienced such a poorly ventilated and odoriferous room—"prostate alley" in St. Marys Hospital could not hold a candle to it! We were tired, so we slept reasonably well, though occasionally we could hear men leaving their bunks to visit the outdoor facility. The creak of the bed springs was audible, even above the noise of some of the other woodsmen who had awoken for similar purposes and then decided to have a smoke or a chew of tobacco while sitting on the side of their bunk. The tinkling sound we heard was due to globs of spit striking the inside of a tin can located beside each lower bunk for that and probably other emergency purposes.

The next night was difficult for me for a different reason. At our camp site on the hunting grounds, a canvas lean-to was set up for our protection and a log fire was built in front of it. The fire was built so that the heat would be reflected on us by the lean-to, but novice that I was, even in my sleeping bag placed next to Dr. Judd's under the lean-to, I found it difficult to keep warm and to sleep. The next night was worse. While searching for moose, we trod over broken tree branches and rough land; however, I seemed to stumble more than the others, probably because I was inexperienced and overly tired. Judd and Plummer both recognized what was happening and so both of them said to me that evening: "You didn't sleep too well last night, did you? Did you get cold?" When I said "Yes," they said *they* had been too warm and they were going to put my sleeping bag between theirs. That night I was much warmer and more comfortable and was able to sleep through the night. Such were my colleagues.

On arrival in Hibbing, having walked 98 miles in eight days—as measured by Dr. Plummer's pedometer—we registered at a pleasant hotel. Our appearance on arrival was deceptive, and two young ladies, who were waiting in the lobby to meet some of the woodsmen coming in for rest and recreation, spotted us. The decision had been made that Dr. Plummer and I would occupy one room and Dr. Berkman and Dr. Judd another. The rooms were around the corner from each other. I was in the bathroom soaking in a large tubful of hot water and Dr. Plummer was reading while awaiting his turn to bathe when there was a knock at the door. Dr. Plummer opened it. A woman's voice said, "Is this Mr. Jones?" Dr. Plummer said, "No." She said, "Would you like my friend and I to come in?" Dr. Plummer stuttered (I had never heard him stutter before) and said, "No, we are very tired, but go around the corner to the first room you come to where two of our friends are located. Just knock on the door and walk right in. They might be interested in seeing you."

The next morning Dr. Berkman told me that Starr Judd was taking a bath when the two girls opened the door and walked in. Dr. Judd yelled out, "What goes on here!" Dr. Berkman asked the girls what they wanted and they said, "One of your friends who has the room around the corner sent us over here and we were told to ask for a Mr. Brown and a Mr. White." Dr. Berkman replied, "Well, I am sorry but I'm Dr. Berkman and Dr. Judd is taking a bath." Whereupon one of the women became flustered and said, "You mean Dr. Judd from the Mayo Clinic?" Dr. Berkman said, "Yes." She was speechless for a few seconds and said, "Dr. Judd operated on my mother for cancer of the stomach and saved her life. I am so sorry but we didn't know who you were. We thought you were men who had been up in the woods for several weeks." They both quickly left the room.

A quiet, modest, generous great American, Starr Judd loved his family and they loved and admired him. So, too, did his closest friends and especially the hundreds of Mayo Foundation Fellows who worked with him. His popularity among members of the medical and surgical professions was apparent by his election to the Presidency of the Minnesota State Medical Association and the American Medical Association and to membership in our most noted invitation societies. He was generous and kind and, though he might infrequently differ with others (including members of the Mayo Board of Governors), he would not allow himself to be engaged in acrimonious debate; although he might at infrequent times forcibly express his opinion and differ with some of the Mayo Clinic's policies, he would always, as Mr. Harry Harwick has said, "go along with us." Dr. Judd was a life-member of the Board of Governors and the Mayo Association for Medical Education and Research (now the Mayo Foundation), but I believe that he, like Dr. Charlie, was not particularly interested in the administrative activities of the Mayo Clin and Foundation. Surgery in all its aspects wa Starr's forte and his love. As if to make know his feelings about surgery, in 1933 he endowe the E. Starr Judd Lectureship in Surgery at th University of Minnesota Medical School. D Dean Lewis, Starr Judd's close friend and Professor of Surgery at Johns Hopkins Medica School, was selected as the first Judd Lecture in 1934. In 1941—six years after the death o Starr Judd and five years after the death of Henr Plummer—the Mayo alumni initiated the Judd Plummer Lectureship at the Mayo Clinic to hono both Judd and his colleague, Dr. Henry Plumme Dr. Thomas M. Joyce, a personal friend of bot and an early surgical assistant and Mayo Alumnu who had become Professor of Surgery at the University of Oregon, was chosen as the first Judd Plummer Lecturer. Both the Judd-Plummer an the E. Starr Judd Lectures have continued to b given at regular intervals.

Dr. E. Starr Judd's great surgical caree spanned only 31 years, but the memory of hin and his accomplishments continue to live an his star will continue to shine brilliantly for al time among the galaxy of other fine and accomplished members of the Mayo Clinic and it Graduate School of Medicine of the Universit of Minnesota.

Dr. Edward D. Henderson

Dr. Edward D. Henderson, Rochester, Minnesota, was elected Second Vice President of the American Academy of Orthopaedic Surgeons at its annual meeting in Dallas.

Under Academy policy he will succeed to the posts of First Vice President in 1975 and President in 1976.

He is consultant in orthopaedic surgery, Mayo Clinic, and professor of orthopaedic surgery, Mayo Graduate School of Medicine. He is also a member of the Board of Governors, Mayo Clinic, and the Board of Trustees, Mayo Foundation.

Dr. J. Minott Stickney

The Executive Committee of the Zumbro Valley Medical Society announced the appointment of Dr. J. Minott Stickney as Executive Secretary of the Society effective February 1, 1974. The office of the Zumbro Valley Medical Society is located at S-1, Mayo Building, Rochester, Minnesota 55901. Dr. Stickney is replacing Dr. Robert E. Fricke who is retiring from this position after 16 years.

Employment for Patients with Diabetes

E. B. COHEN, M.D.* and LEONARD MASTBAUM, M.D.*

Many changes in employment opportunities, compensation laws and drivers' icensure for diabetics in Minnesota have appeared in the last ten years. A knowldgeable, cooperative, primary physician can help his diabetic patient's employnent problem by providing reports to industry or state agency and cooperating vith industrial and government medical departments in placement and diabetes nanagement. Diabetics are employable; they can drive vehicles; and they have etter than average employment records. They need help in selection of jobs for vhich they are suited.

THE PAST TEN YEARS in Minnesota have seen nany changes in employment opportunities, comensation laws, and drivers' licensure for diabetics. None of this helps the individual patient unless a knowledgeable primary physician is able to provide history and physical reports to industry or state agency; later to follow-up by cooperating with industrial and government medical departments in placement and diabetes management. He should also be able to give testimony in helping to wipe out remaining pockets of employment discrimination. An informed medical adviser is the key to employment progress for the diabetic patient.[6,11-15]

Diabetics are Good Employees

A recent Minnesota State Medical Association statement says: "Persons with controlled diabetes, having no serious complications, are good employment risks. Such diabetics should not be classified as vocationally handicapped. They are capable of performing satisfactorily in most positions, if other wise suited by way of training and physical qualifications. The presence of diabetes does not, of itself, constitute a categoric reason for unemployability. When physical and mental qualifications . . . help determine employability, the final decision should always be made on an individual basis. . . . With better knowledge of diabetes control, diabetics are increasingly suitable for employment. The experience of hundreds of companies currently employing persons with diabetes indicates that often diabetics, being self-disciplined and well balanced, become their most outstanding workers, and productive, reliable employees".[1] Surveys available in the literature of both industry and medicine document the employability of the diabetic.[2-4,9]

One such study was an analysis of questionnaires returned by 127 employers whose firms employed 1,800,000 people. Sixty-nine percent of the firms employed diabetics. Only 6% of these respondents described their experience as to reliability and absenteeism as unsatisfactory. Eighty-seven percent allowed diabetic employees to participate in insurance and other benefits, and continued to employ those who developed diabetes after they began work. Sixty-six percent reported absenteeism records in their employees with diabetes "as good as" or "better than" the general average.[2]

The Philadelphia Electric Company, employing over 100 diabetics, reported during a period of 18 years that absenteeism among the diabetics was 33% less than that of other employees.[3]

In a 1971 survey, 142 employers reported that 87.5% of employees with diabetes were "no worse than" (81.9%) or "better than" (5.6%) those who did not have diabetes, with respect to absenteeism and reliability.[4]

Educational Attainment of Diabetics is Superior

One hundred-sixteen young people with diabetes who had attended Camp NYDA (New York Diabetes Association) were followed for ten years. The study started at about age 16 and continued to age 26. They were selected from rural and

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*Clinical Assistant Professor of Medicine, University of Minnesota Medical School, Minneapolis:.
See editorial, page 221.

urban New York settings. After ten years, of 116 teenagers with diabetes, 109 had completed high school; 79 were in college, had completed college, or were postgraduate students; and 30 had completed vocational training courses.[5] Educational achievement was found to be greater than that shown in most studies in the general population (or even in most studies of economically favored segments of the community).

Civil Service Jobs are Open to Diabetics

A recent survey of 33 public Civil Service Jurisdictions showed that six "hire individual diabetics without prejudice"; eleven for "sedentary or non-hazardous jobs mainly"; seventeen for jobs "individually determined". Five refused to hire persons with diabetes. The total number of responses adds up to more than the 33 communities surveyed, because six of the respondents checked several answers.

In 1969, the Hennepin County Civil Service Commission, which in the past had a policy of employment discrimination against diabetics, followed the example of most of the communities studied, and opened up for employment 600 classes of positions; excluding only 45. The Commission concluded: "The exclusions in general are not populous classes, except for fire-fighter and patrolman. The classes that are excluded are classes that involve as a primary responsibility such duties as climbing to high places, working around power driven machinery, working in sewers, which involves wading in pouring water, and the like".[6]

The United States Civil Service Commission policy on employment of diabetics states: "All diabetics who have achieved a reasonable control of the condition are eligible for Federal employment with proper placement. Proper placement will be based on the severity of the condition and the medication required for control".[7]

Prior to 1941, persons who were known to have diabetes mellitus were not acceptable for Federal employment. Since that time physical standards have been modified to permit the acceptance of diabetics providing they are able to perform the duties of their positions efficiently, without hazard to themselves or others. Diabetics who can achieve satisfactory control by diet alone, diet and an oral medication, or with diet and a moderate amount of insulin are eligible for all Federal positions except the most demanding. Diabetics who require substantial amounts of insulin should not be placed in positions in which a sudden loss of consciousness would endanger themselves and others. This hazard precludes the assignment of the relatively severe diabetics to positions which involve working at heights, around dangerous power driven machinery, or the operation of a motor vehicle. Proper control and absence of complications are major considerations.[7]

The United States Civil Service Commission recommends: "Diabetics can more readily maintain a stable control if they are not subject to rotating shifts or work which requires irregular heavy physical demands. Diabetics should carry cards or tags at all times identifying their condition. Diabetics should be under the guidance of a clinic or personal physician and should report periodically for physical examination and medical evaluation".[7]

A brochure entitled "Diabetics are Desirable Workers"[10] has recently been distributed by the American Diabetes Association recommending guidelines similar to those of the United States Civil Service Commission.

Licensing Diabetics to Drive Cars

Before 1963, Minnesotans with diabetes came under provisions of a statute dealing with unpredictable loss of consciousness (such as occurs in epilepsy). Those who had accidents, or "dangerous driving incidents" were subject to automatic two-year license suspensions. The Minnesota Highway Department then adopted new guidelines suggested by the Advisory Committee on Diabetes of the State Medical Association.

Following accidents, if information received from drivers and doctors is correct, it appears that medical follow-up and patient cooperation both improve, for a second loss of control is unlikely, and very few have further incidents.[8]

Diabetes Vs. Types of Assignments

Over 90% of the four million diabetics in the United States have "maturity onset" type of diabetes. About 20% of these use insulin.[8] There should be little hesitation to hire such applicants (both the minority who need some insulin by injection, and the great majority who are regulated on diet alone, or diet plus oral medication).

What about the ten-percent (or less) of all iabetics who have “juvenile diabetes”? They alnost all take insulin. Some of them have untable diabetes, and 2% or 3% are “brittle” impossible to keep optimally controlled). These ob applicants are a challenge to personal phyicians and to management in two ways: sensible election and proper job placement. Those who re well regulated (the conscientious ones among he “more severe” diabetics are often the best ontrolled) have been reported to be outstanding nd well-disciplined employees. Minor precauions are needed. Avoid irregular shifts which make eating hours unpredictable; select assignments least likely to cause injury; insulin-users should not operate hazardous machinery; insulin taking workers should carry candy or fruit, in case of symptoms suggesting insulin reaction.

In many states having Second Injury laws, hiring diabetic workers gives the employer an insurance advantage. Where the law is intended to cover diabetics (as in Minnesota), the state guarantees medical expense beyond a fixed sum, if the diabetes is a factor in causing the injury, or delays recovery therefrom.[15]

All applicants for a job must be judged as to physical fitness and vocational training (or educability). Employers should consider, in diabetic applicants, the following: “(1) Severity of the diabetes. (2) Regulation and control of the diabetes. (3) Cooperation of the patient in submitting to regular periodic examination and care of his disease. (4) Cooperation and understanding of industrial problems by the physician treating the diabetes”.[9]

A suggested pre-employment form for job applicants with diabetes is appended.

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15. Personal communication from James Pomush, Commissioner, Minnesota Department of Labor and Industry, 1969.

Diabetes Biography—Pre-Employment Form
Applicant's Statement

Name:
Address:
Phone:
Marital Status:
Birthdate:

Medical supervision:
Physician .... Phone ....
Address ....
Frequency of visits to Physician ....
Date of Onset of Diabetes ....
Diet: .... Can you fit cafeteria meals into your diet?.......... Meals carried to work?..........
Insulin:
Dosage(s) If none, so state ....
Type(s) .... Time(s) ....
Who injects it? ....
For insulin takers only
Insulin (Hypoglycemic) Reactions: Is food carried at all times? ....
Date of last reaction ....
Number in past year ....
Usual time of day .... Severity ....
Need for assistance ....
Ever cause unconsciousness: yes........ no ....
Last time ....
Antidiabetic tablets:
Drug name and dose ....
Number tablets per day ....
Ever had hypoglycemic reaction (due to tablets): yes.......... no..........
Urine Tests:
Average Number Daily ....
Method: Clinitest...................
Tape...................
Other...................
Usual Results: 0- 1+ ....
0- 4+ ....
Often 4+ ....
Health Record:........
Approximate number of days absent from work or school in past two years ....
Reasons ....

Diebetes Health Summary
Physician's Statement

Applicant ....
Address ....
Date of Birth ....
Date of Last Complete Examination ....

Diabetes History.

Age of discovery ....
Under my care since ....
Type of Diabetes: Mild........ Moderate........ Severe........
Stable and easily controlled ....
Unstable and difficult to regulate ....
Cooperation:
In medical supervision and treatment:
good to fair ....
fair to poor ....
In diet: good to fair .... fair to poor ....
questionable ....
How often do you see patient? ....
Date of last visit ....

Insulin: Type.......... Dose range.......... to .... units daily.
Number of injections daily ....

Control:
Reactions: None ....
Mild and easily controlled without assistance ....
Severe reactions in past 12 months ....
Date of last severe reaction ....
List the last 4 or 5 blood sugars ....
Fasting .... Postprandial ....
Ketosis: Yes ( ) No ( ) Frequency ....
Date of last episode ....
Oral Hypoglycemic Agent: Type .... Dose ....
Reactions ....

Associated Condition:

	Yes	No	Duration	Severity
Ketosis	( )	( )	....	....
Cataract	( )	( )	....	....
Retinopathy	( )	( )	....	....
Nephropathy	( )	( )	....	....
Neuropathy	( )	( )	....	....
Peripheral vascular or other lesions of the lower extremities	( )	( )	....	....
Coronary disease	( )	( )	....	....
Cerebral vascular disease	( )	( )	....	....

Health Record:

Absence from work or normal activities in past two years:
Frequency ....
Duration ....
Reasons ....
Other significant medical impairments: ....
....
....

Physical Findings:

Height............ Weight .... B.P............ P............
Weight change in past year ....
Eyes: Visual Acuity Right................. Left.................
Cataracts? Yes................ No...............
Retinopathy? Yes................ No...............
Proliferative ( )
Non-Proliferative ( )
E.N.T. ....
Chest ....
Heart ....
Abdomen ....

Peripheral Pulse:

	Right Reduced	Right Normal	Left Reduced	Left Normal
Carotids	....	....	....	....
Radial	....	....	....	....
Ulnar	....	....	....	....
Femoral	....	....	....	....
Post. Tibial				
Dorsalis Pedis	....	....	....	....

Nervous System:

Sensation (Pin-Prick)
Hands................................. Feet.................................
Motor Strength
Hands and Arms................ Feet and Legs................
Coordination
Hands and Arms................ Feet and Legs................
Other ....

Skin:

Ulcers ....
Poor Healing ....
Other ....

Physician's Assessment of Applicant

Cooperation ....
Reliability ....
Control of Diabetes ....
Maturity and Emotional Adjustment to His Diabetes ....
....

Job capabilities; based on Medical Evaluation:

1. Any job for which otherwise qualified. ....
2. Any job for which otherwise qualified except for hazardous jobs. ....
....
3. Sedentary jobs only. ....
4. Unemployable. ....

Special Limitations: ....
....
....

Gonorrhea at a Teenage Medical Service

ELIZABETH JEROME, M.D.;[*] BETTY FLEMING, PH.D.;[†]
MARGARET MILLER, M.T. ASCP;[‡] ESTHER MILLER, M.T. ASCP;[#] and MARY ALICE McMONIGAL[§]

Gonorrhea among the sexually active youth is such a serious problem that the Teenage Medical Service staff devotes its afternoon time exclusively to testing for gonorrhea.

THIS REPORT describes the result of a one-year study for gonorrhea detection in Minneapolis teenagers. These teenagers, ages 13 to 20, were evaluated by physicians at the Teenage Medical Service (TAMS), an out-patient clinic of the Minneapolis Children's Health Center. Since physician referral is not necessary, the teenage patients learn of this clinic, for the most part, by word of mouth or from the mass media. Forty-five volunteer physicians, serve the clinic along with 150 other volunteers including nurses, bacteriologists and laboratory technologists. The clinic is operational during evening and daytime hours for approximately 40 hours per week. Most patients are seen for reasons of birth control, suspected pregnancy, or venereal disease.

TABLE 1
Female Patient Examinations
Reported Positive For Gonorrhea

Type of Patient	Number	Positive	Percent
Birth Control	2176	30	1.4
Suspected Pregnancy	1168	17	1.5
Cure Check	248	16	6.5
Others	1979	178	9.0
Total	5571	241	4.3

Male Patient Examinations
Reported Positive For Gonorrhea

Type of Patient	Number	Positive	Percent
Male	514	71	13.8

The study period lasted from January 1, 1972 through December 31, 1972 and included 6,085 patients. 1,492 (26.8%) of the 5,571 females in this study were initially seen in the birth control clinic, whereas the remaining 4,079 were from the general clinic. All 514 male patients came to the general clinic. Most males were referred by female partners who already had a positive diagnosis of gonorrhea.

In each case endocervical and/or urethral swabs were taken. These were smeared and cultured on Thayer-Martin medium. The culture plates were placed in a CO_2 incubator at 36 degrees centrigrade for 24-48 hours. In the early phases of this study rectal cultures were performed on all females in addition to the standard endocervical culture while in the latter part of this study only endocervical cultures were performed on females. Patients who were known male homosexuals had both rectal as well as urethral cultures.

TABLE 2
Results in 514 Males

	Reported Positive		Reported Negative		Percent of Total	
Exams	Number	Percent	Number	Percent	Number	Percent
Symptomatic	60	21.5	219	78.5	279	54.3
Asymptomatic	11	4.6	224	95.4	235	45.7
Total	71	13.8	443	86.2	514	100.0

TABLE 3
Results in 1979 Female Examinations In The Regular Clinic Excluding
Birth Control Patients, Pregnancy and Cure Check

	Reported Positive		Reported Negative		Percent of Total	
Exams	Number	Percent	Number	Percent	Number	Percent
Symptomatic	114	10.5	963	89.5	1011	54.4
Asymptomatic	64	7.1	838	92.9	902	45.6
Total	173	9.0	1801	91.0	1979	100.0

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[*] Director, Teenage Medical Service (TAMS).
[†] Bacteriologist, Teenage Medical Service.
[‡] Bacteriologist, MT ASCP, Teenage Medical Service.
[#] MT ASCP, Teenage Medical Service.
[§] Laboratory Assistant, Teenage Medical Service.

Results

In Tables 1 through 4 are the test results divided by percentage positives (Table 1), symptomatology (Tables 2 and 3) and results of smears and cultures (Table 4).

Discussion

The minimum rate of gonorrhea reported in Minnesota for 1972 was 21.9 per 10,000. The Minnesota State Board of Health considers an area to have a high incidence rate of infection if there are 30 to 220 cases per 10,000 population. The rate of gonorrhea infections in 1972 at TAMS was 510 per 10,000. The figures cited at TAMS support the argument for intense testing programs among sexually active young people.

It is generally assumed that cultures and smears in males agree. In this study 17% failed to show agreement. Because of this, there is need to make both smears and cultures on all males. Whenever smears from males showed numerous PMN's with no organisms visible and culture was negative, non-specific urethritis was diagnosed.

Gram-stained smears alone from females are generally considered to be unreliable, since other organisms can be difficult to differentiate from Neisseria gonococcus. In our clinic, culture on Thayer-Martin medium is considered to be much more reliable than the gram-stained smear. Treatment is withheld until culture reports are available.

Gonorrhea among the sexually active youth presents such a serious problem that five afternoons per week our staff devotes its time exclusively to testing for general infections, for individual patient conferences and to tracing "contacts" so that further spread can be minimized with treatment. In addition, through conferences in groups of 10 to 20 patients, we emphasize that all sexually active patients should have cultures and slides repeated with each change of sex partner or when doubts of the partner's fidelity arise.

TABLE 4
Male Examinations; Smears and Cultures

	Smear +	Smear —	Total
Culture +	53	7	60
Culture —	4	443	447
Total	57	450	507*

---

*Plus 7 positive cultures—no slide taken.

Female Examinations; Smears and Cultures

	Smear +	Smear —	Total
Culture +	95	120	215
Culture —	7	3838	3845
Total	102	3958	4050*

---

*Plus 19 positive cultures—no slide taken.

University of Minnesota
Continuing Education Course

The Department of Surgery of the University of Minnesota announces its annual symposium in Surgery: "Surgery of the Liver, Biliary Tract, and Pancreas," May 29 through June 1, 1974 at the Leamington Hotel in downtown Minneapolis. This program is designed primarily for surgeons and is presented under the direction of Doctors John S. Najarian and John P. Delaney of the University of Minnesota Medical School. Guest faculty members will include: H. Joachim Burhenne, Ben Eiseman, Marvin L. Gliedman, John M. Howard, Frank G. Moody, Hans Popper, Seymour Schwartz, Sheila Sherlock, Rodney Smith, Thomas E. Starzl, W. Dean Warren, Thomas T. White, and Robert M. Zollinger. Further information contact: Dr. John P. Delaney, Box 89, University of Minnesota Hospitals, Minneapolis, Minnesota 55455 or by calling (612) 373-8807.

121st Annual Meeting Minnesota State Medical Association

May 16-17, 1974

Why Have an Annual Meeting?

THIS YEAR THE Association will hold its 121st annual meeting. Times have changed since that first one when a handful of physicians from the Minnesota Territory got together to share ideas, help solve each other's problems and enjoy each other's company.

The idea of getting together once a year to keep in touch, not just on a social level, but on a professional level as well, caught on—and we've grown up.

The world has become more involved, the practice of medicine has become more involved, and so have the activities of the Association.

Today, more than ever, our fellow physicians are being called upon to actively support the endeavors of the Association. The business of the House of Delegates promises to be of great interest and importance to the physicians of the state; many issues, including the quandary over HMO's and PSRO's, are at stake and must be resolved. Input from the WHOLE membership is needed to assure the delegates and to assist them in their serious tasks; you are welcome to attend the open hearings of the reference committees as they tackle the policy-making issues that are of importance to us all.

Advances and breakthroughs are occurring in medicine faster than it seems possible to keep up. Never has medicine and the medical profession been so questioned. The scientific program—"Crisis Medicine/Medicine in Crisis" has been planned to deal with these problems confronting physicians today. The two-day session promises to be of high academic and scientific appeal, accredited by the AMA and approved by the AAFP for 13.5 prescribed hours in Category 1 of the Physicians Recognition Award.

The Scientific program's first session will be a result analysis of the controversial coronary bypass procedure followed by a panel discussion of the crisis in extraordinary health care, who makes the decisions, and who has to justify them. This promises to be a fast paced, give-and-take session, involving well-known figures in such fields as: neonatal care, renal transplants, chemotherapy, and cardiology. Workshops are scheduled for portions of both days, introducing new topics, some old, but with new approaches: Chemical Dependency, Biopsies, The Scanner, Office Obstetrics, The Acute Painful Joint, a different view on mental retardation . . . and this is just a sample!

Again this year the program on surgery and surgical trauma will be sponsored by the Minnesota Chapter of the American College of Surgeons, and it portends to be as interesting, informative and excellently presented as their programs in the past.

Luncheons on May 16 and 17 are part of the scientific program and very worthwhile. We're sure that our membership and their wives will find the topics relevant to their lives and the speakers stimulating. On Thursday, Clark Vincent, Director of the Marital Health Clinic at Wake Forest University, will discuss the crises unique to medical marriages, and on Friday, Roger Linnemann, President of Radiation Management Corporation, will deal with the benefits and problems of nuclear power in conjunction with its effects on the environment.

Sessions on the personal crises of physicians and how these affect their professional roles will prove to be timely topics, along with a session on human sexuality geared for the family physician.

Don't forget to visit the exhibits, meet the exhibitors; this is a great opportunity to gather the latest information on services, medications, techniques, publications, etc.

We know that all work and no play makes Jack a dull doctor . . . so play there will be! One of the best golf courses in the area, Northland Country Club, will be the setting of this year's golf tournament. The Duluth Indoor Tennis Club is the site of the Association's tennis tournament. Trophies and prizes will be awarded at all tournaments. This year we've even brought back the bridge tournament for all you cool, methodical thinkers.

There are twenty-one physicians who will be honored and welcomed into the Fifty Club in celebration of fifty years of practice in Minnesota. Fifty years of service and dedication is quite a feat! We're looking forward to that moment during the Banquet when the name of the recipient of the Association's highest honor, The Distinguished Service Award, will be announced. A great moment in the life of a great colleague. And there's more—the winners of the President's Awards. There is that moment, too, when we congratulate our President on a job well done and welcome in his successor.

So why have an annual meeting? . . . To share ideas, help solve each other's problems, and enjoy each other's company.

Duluth May 16 and 17—come on!

Robert D. Semsch, M.D.
Scientific Assembly Committee Chairman
and
William E. Jacott, M.D.
Local Arrangements Committee Chairman

Community Referral Sources

A number of sources are available to physicians seeking information on community service organizations for referral purposes. The following is one such source:

Bloomington Public Health-Family Planning and V.D. Clinic
10100 Morgan Avenue South, Bloomington, Mn.
Phone: 881-5811 Clinic: 888-9988

Services	Days/Hours	Eligibility	Fees
*Family planning and birth control	Clinic hours only: Mon. & Thurs./ 5-9 p.m.	None	Examination is based on ability to pay plus cost for prescriptions
Pregnancy testing	"		
*V.D. detection and treatment	"		
	Office hours: Mon.-Fri./ 8 a.m.-5:30 p.m.		

Average number of people served per month: 160
Age range: No limitation on age.

Community service directors are available from the Community Health and Welfare Planning Councils in Minneapolis and St. Paul. For a directory of metropolitan youth-serving agencies, The Catalogue can be obtained from Enablers, Inc., 1238 Baker Building, 706 Second Avenue So., Minneapolis, Minnesota 55402.

Classified Advertisements

Classified advertising rates are thirty (30) cents a word; minimum monthly charge $7.50; key number, $1.00 additional.

Replies to advertisements with key numbers should be mailed in care of Minnesota Medicine, 375 Jackson, St. Paul, Minn. 55101.

THE MIDELFORT CLINIC is seeking associates in the following areas: (1) Allergy; (2) Family Practice; (3) Internal Medicine. This is an opportunity to join a 25-man Wisconsin group located in college community of 46,000 with excellent hospital facilities. For further information, contact D. R. Griffith, M.D., Midelfort Clinic, Eau Claire, Wisconsin.

MMI ANNOUNCES STATE-WIDE REGISTRATION. We are presently registering physicians who: (1) Desire coverage for their practice on weekends, or periods of one week to several or more months—OR—(2) Are available to do Locum Tenen on weekends, or periods of one week to several or more months. Write or call today for a registration form. MIDWEST MEDICAL, INC.—Lakeland, Minn. 55043—Phone (612) 436-5161.

INTERNIST-FAMILY PRACTITIONER to join three Family Practitioners and one Board Certified Surgeon in Incorporated group practice. Only 60 minutes north of the Minneapolis-St. Paul area with easy access to lakes and outdoor sports. Facilities include New Clinic, 63 bed general hospital with ICCU and 87 bed nursing home, all new. Call or write: Larry J. Brettingen, M.D., 224 7th St., Mora, Minnesota 55051, Ph. (612) 679-1313.

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RIVERS EDGE MEDICAL CLINIC—Farmington, Mn. needs two additional General Practitioners to practice in a nearly new Clinic, Hospital and Nursing Home. Fast growing area just 45 minutes from St. Paul-Minneapolis. Metropolitan advantage with Community living. Contact M. H. Hunter, M.D. (612) 463-7181.

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FOR SALE—Lucrative solo General Practice. Office completely furnished, will leave records and introduce. Located in a city of 2500 pop., midway between the Twin Cities and Rochester. Excellent schools and recreation facilities. Will rent or sell building. Dr. retiring.—Dr. Marland R. Williams, Box 98, Cannon Falls, Minn. 55009. 1-507-263-2511, office; 1-507-263-2050, residence.

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(Continued to Page 250)

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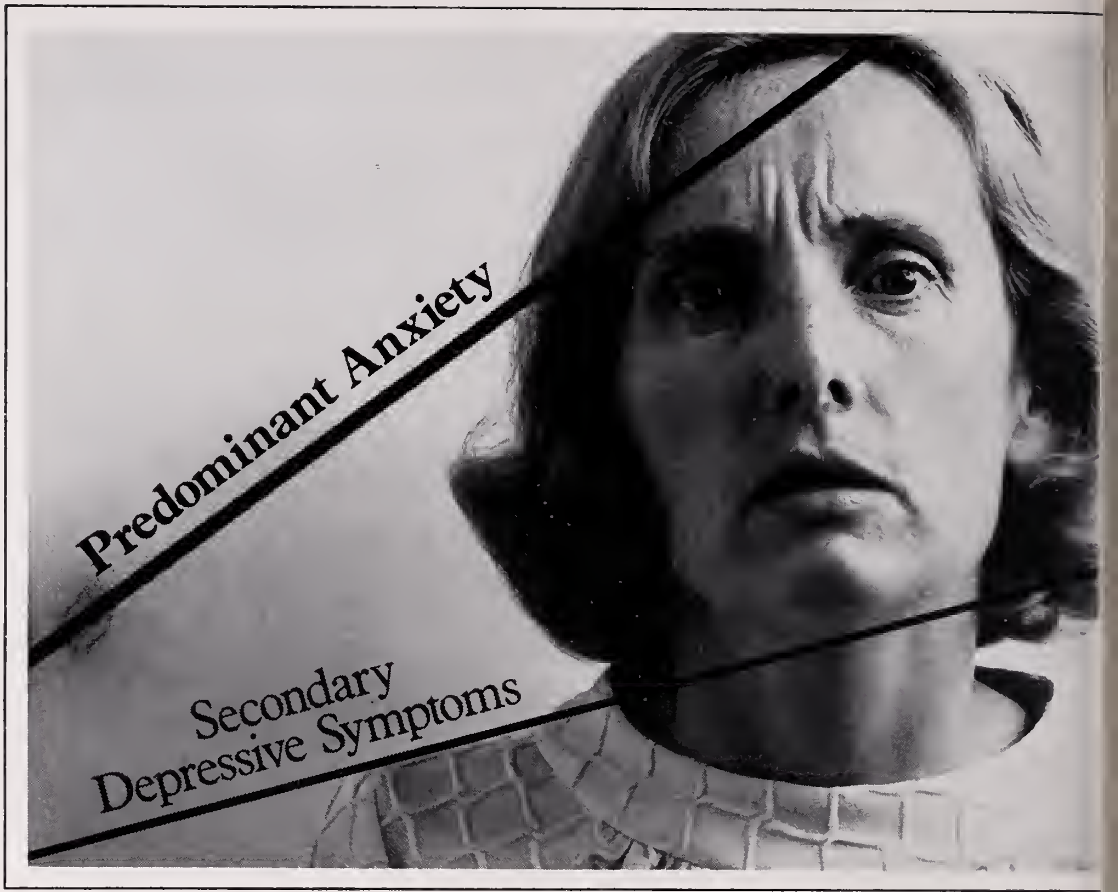

This psychoneurotic often responds

Before prescribing, please consult complete product information, a summary of which follows:

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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal m be associated with temporary increase in frequency and/or severi of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdraw symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomit and sweating). Keep addiction-pr individuals under careful surveillance because of their predisposit to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

When you determine that the depressive symptoms are associated with or secondary to predominant anxiety in the psychoneurotic patient, consider Valium (diazepam) in addition to reassurance and counseling, for the psychotherapeutic support it provides. As anxiety is relieved, the depressive symptoms referable to it are also often relieved or reduced.

The beneficial effect of Valium is usually pronounced and rapid. Improvement generally becomes evident within a few days, although some patients may require a longer period. Moreover, Valium (diazepam) is generally well tolerated. Side effects most commonly reported are drowsiness, ataxia and fatigue. Caution your patients against engaging in hazardous occupations or driving.

Frequently, the patient's symptoms are greatly intensified at bedtime. In such situations, Valium offers an additional advantage: adding an *h.s.* dose to the *b.i.d.* or *t.i.d.* schedule can relieve the anxiety and thus may encourage a more restful night's sleep.

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o Valium® (diazepam)

Precautions: If combined with her psychotropics or anticonvulnts, consider carefully pharmalogy of agents employed; drugs ch as phenothiazines, narcotics, rbiturates, MAO inhibitors and her antidepressants may potente its action. Usual precautions dicated in patients severely deessed, or with latent depression, with suicidal tendencies. Observe ual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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another type for Tylenol
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When the post-T & A patient requires an analgesic, a new problem arises. Hemorrhagic tendencies following the use of aspirin after tonsillectomies have been reported![1,2] In a patient who "...has recently undergone a surgical procedure or has another underlying hemostatic defect, aspirin ingestion may cause significant bleeding....Aspirin is absolutely contraindicated in such situations. Acetaminophen...could replace aspirin in these instances."[3]

The post-T & A patient is only one of several 'types for TYLENOL'—that is, patients who should avoid aspirin. Considering all of them, wouldn't it provide added safety (as well as added convenience) to recommend TYLENOL (acetaminophen) routinely for simple analgesia?

References: 1. Reuter, S. H., and Montgomery, W. W.: Arch. Otolaryng. *80*:214-217 (Aug.) 1964. **2.** Osol, A., et al., ed.: The United States Dispensatory and Physicians' Pharmacology, ed. 26, Philadelphia, J. B. Lippincott Co., 1967, p. 171. **3.** Schwartz, A. D., and Pearson, H. A.: J. Pediat. *78*:558-560 (March) 1971.

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President's Letter

Rocky Mountain Honeymoon

A newly-elected chief of staff of any hospital of reasonable size may be subjected early in his tenure to the week-long conference on hospital-medical staff relations sponsored by the American Hospital Association and conducted by the University of Colorado in the YMCA Camp at Estes Park. There, in a fiercely Christian setting where one must not only smuggle in his bottle of Scotch, but even keep it hidden under the bed, one breathes fresh mountain air, eats good YMCA food, and digests (or indigests) propaganda designed to set straight his thinking on hospital staff relationships. Some pretty good ideas are revealed; but much that is given him is biased; some is nonsense;—and some, purely and simply inaccurate. He might hear extolled the virtues of the corporate system of hospital management; he probably will have described gross misinterpretations of that favorite of the party line, the Darling case;* he will certainly listen to a physician who is not a graduate of one of our United States medical schools and who has never been a practitioner of medicine in our country, pontificate about hospital-staff relationship. Some of the better lines of this gentleman include "the administrator is the board of trustees in residence"; "Access to the board from the medical staff is through the hospital administrator". And his superlative line "these things are non-negotiable and non-debatable." The fact is that in this uncertain life everything is debatable and hence everything is negotiable.

It is a lovely week in a lovely valley. The mountains are beautiful, the camp is well equipped, and the company pleasant. But, one wonders at the reason for all this expenditure of the dollars of our sick patients—whether there is a need to educate physicians in the system, or whether indeed there is something about the administrative structure of hospitals that makes it necessary to do a Madison Avenue public relations job on new staff officers. After all, the system started simply many centuries ago with the lone Shaman ministering to the members of his tribe with wisdom and skill. The increasing complexity of society and the burden of increased knowledge made specialization necessary, so the Shaman became physician, or lawyer or priest—the three learned professions of ancient times, and the physician continued to be a lone practitioner treating patients in his home or theirs. Temples of Greek and Roman days, and hospitals of Christian Europe from about the fourth century, or of the great Arabic kingdoms from somewhat later, were places of refuge for the homeless, the sick poor, the blind, and the leper. It was only with the expansion of knowledge following the invention of the printing press, and later its major acceleration in the 19th century, that the physician brought his patients to a hospital rather than treating them at home. The practitioner treating sick patients in the hospital gathered around him a variety of ancillary helpers. The newest of these is the hospital administrator, who was introduced to bring principles of modern scientific management into this now highly complex group. Unfortunately, there are ambitious persons, hospital trustees, administrators or whatever, who are not content to contribute their skills, but who are impelled by a desire to expand, to increase and even to take over the structure. They fail to

(Continued on page 296)

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*Dorrence Kenneth Darling, II -vs- Charleston Community Memorial Hospital, 211 N.E. 2d 253. In this case a hospital was held liable for physician malpractice.

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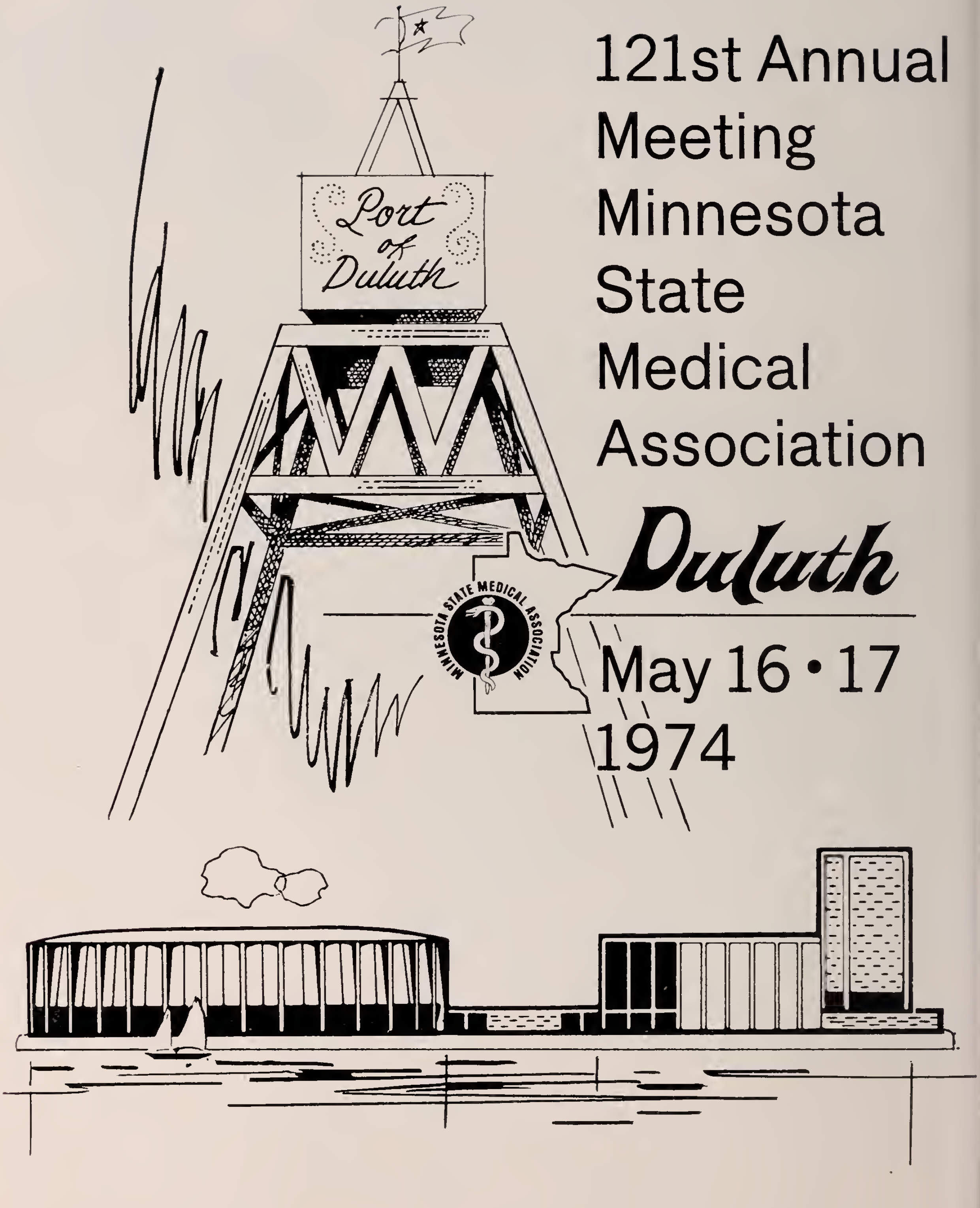
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ore prescribing, see complete prescribing
rmation in SK&F literature or *PDR*. The
owing is a brief summary.
ications: Edema associated with congestive
rt failure, cirrhosis of the liver, the nephrotic
drome; steroid-induced and idiopathic
ma; edema resistant to other diuretic therapy.
o, mild to moderate hypertension.
traindications: Pre-existing elevated serum
assium. Hypersensitivity to either com-
ent. Continued use in progressive renal or
atic dysfunction or developing hyperkalemia.
rnings: Do not use dietary potassium supple-
nts or potassium salts unless hypokalemia
elops or dietary potassium intake is markedly
aired. Enteric-coated potassium salts may
se small bowel stenosis with or without
eration. Hyperkalemia (>5.4 mEq/L) has
n reported in 4% of patients under 60 years,
12% of patients over 60 years, and in less
n 8% of patients overall. Rarely, cases have
n associated with cardiac irregularities.
cordingly, check serum potassium during
rapy, particularly in patients with suspected
confirmed renal insufficiency (e.g., elderly or
betics). If hyperkalemia develops, substitute
hiazide alone. If spironolactone is used
ncomitantly with 'Dyazide', check serum
tassium frequently—both can cause potassium
ention and sometimes hyperkalemia. Two
aths have been reported in patients on such
mbined therapy (in one, recommended
sage was exceeded; in the other, serum elec-
lytes were not properly monitored). Observe
tients on 'Dyazide' regularly for possible
od dyscrasias, liver damage or other idio-
ncratic reactions. Blood dyscrasias have been
ported in patients receiving Dyrenium
iamterene, SK&F). Rarely, leukopenia,
rombocytopenia, agranulocytosis, and aplastic
emia have been reported with the thiazides.
atch for signs of impending coma in acutely
cirrhotics. Thiazides are reported to cross the
acental barrier and appear in breast milk.
is may result in fetal or neonatal hyperbili-
binemia, thrombocytopenia, altered carbo-
drate metabolism and possibly other adverse
actions that have occurred in the adult. When
ed during pregnancy or in women who might
ar children, weigh potential benefits against
ssible hazards to fetus.
ecautions: Do periodic serum electrolyte and
UN determinations. Do periodic hematologic
udies in cirrhotics with splenomegaly. Anti-
pertensive effects may be enhanced in post-
mpathectomy patients. The following may
cur: hyperuricemia and gout, reversible
trogen retention, descreasing alkali reserve
ith possible metabolic acidosis, hyperglycemia
nd glycosuria (diabetic insulin requirements
ay be altered), digitalis intoxication (in
ypokalemia). Use cautiously in surgical
atients. Concomitant use with antihypertensive
gents may result in an additive hypotensive
ffect.
dverse Reactions: Muscle cramps, weakness,
izziness, headache, dry mouth; anaphylaxis;
ash, urticaria, photosensitivity, purpura, other
ermatological conditions; nausea and vomiting
may indicate electrolyte imbalance), diarrhea,
onstipation, other gastrointestinal distur-
ances. Rarely, necrotizing vasculitis, pares-
hesias, icterus, pancreatitis, and xanthopsia
ave occurred with thiazides alone.
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The Board of Trustees of the American Medical Association

The American Psychiatric Associatio

The Executive Committee of the National Association of Retail Druggists

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J nt Statement on Antisubstitution Laws and Regulations

The purpose of this statement is t affirm the support of the participat- ; organizations for the laws, regula- t ns and professional traditions which p hibit the unauthorized substitution c drug products.

Traditionally, physicians, den- t ts and pharmacists have worked c operatively to serve the best inter- e s of patients. Productive coopera- t n has been achieved through utual respect as well as a common ncern for the ideals of public rvice. This mutual respect has been lected, in part, by joint support er the years for the adoption and forcement of laws and regulations ecifically prohibiting unauthorized bstitution and encouraging joint scussion and selection of the urce of supply of drug products. e basic principles of medical, den- and pharmacy practice are thus ilized and preserved in the interest patient welfare.

The antisubstitution laws have t obstructed enhancement of the ofessional status of pharmacy any ore than they have in and of them- lves guaranteed absolute protec- n from unsafe drugs, or freed ysicians, dentists and pharmacists m their responsibilities to patients. a practical matter, however, such ws and regulations encourage inter- ofessional communications regard- g drug product selection and assure ch profession the opportunity to ercise fully its expertise in drug age, to the advantage of patients.

Physicians and dentists should urged to increase the frequency d regularity of their contacts with armacists in selection of quality ug products, recognizing that economies to patients can be improved through such communication, taking into account the patients' needs. The pharmacist's knowledge of the chemical characteristics of drugs, their mode of action, toxic properties and other characteristics that assist in making drug selection decisions should be utilized to the fullest extent practicable by physicians and dentists in serving their patients.

Since drug product selection entails knowledge derived from clinical experience, the physician's and dentist's roles in product selection remain primary and do not permit delegation of decisions requiring medical and dental judgments. A broader role in therapy will evolve for pharmacists as improved understanding and cooperation among the professions continue to grow.

There has been no evidence that there are convincing reasons to modify or repeal existing laws and regulations prohibiting the unauthorized substitution of another drug product for the one specified by a prescriber. It is our belief that such laws and regulations merit the joint support of the medical, dental and pharmaceutical professions and the pharmaceutical industry.

Add your opinion to the weight of other professionals and send it to your state assemblyman or legislator.

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X-Linked Choroidal Sclerosis

A Stage of Choroideremia

IRVING SHAPIRO, M.D.* and ROBERT J. GORLIN, D.D.S.†

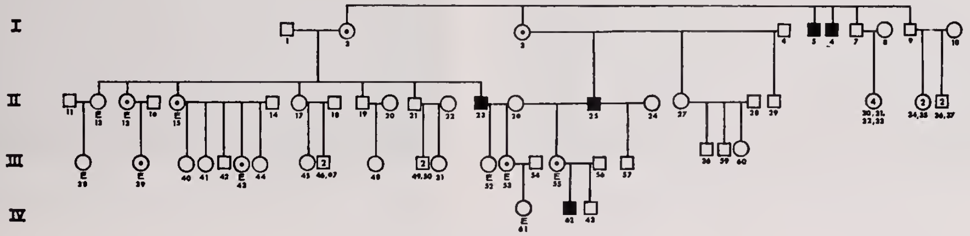
Observation of a large kindred since 1958 has given the authors the opportunity of seeing the transformation of X-linked choroidal sclerosis into choroideremia supporting the hypothesis of other observers that these conditions are stages of the same disorder.

Choroidal sclerosis has been classified into two principal varieties: a central or peripapillary form and a generalized choroidal sclerosis. In this latter type, the atrophic area may involve the entire fundus. Some cases of generalized choroidal sclerosis have exhibited autosomal dominant transmission,[1,2] while most others have manifested X-linked inheritance. It is this latter group of cases which we wish to critically examine.

Although initially separated as a distinct entity,[3] within the past decade, X-linked choroidal sclerosis has been considered the same as choroideremia.[4-6] This evolution in viewpoint has been based upon the great variability in types of choroidal vasculature which has been documented in various members of families with choroideremia.[5,7] Krill and Archer[5] indicated a great range of changes occurring in choroidal vascular atrophy. Initially this atrophy affects the choriocapillaris, but eventually larger vessels become involved, both types upon occasion being seen in the same eyegrounds of a person with choroideremia. Furthermore, different affected members of a single family may manifest mainly one or the other type of atrophy of the choroidal vasculature.

Sorsby and Savory[3] describe two pedigrees. The first manifested classic X-linked choroidal sclerosis. The second was poorly documented pictorially and one cannot tell with certainty whether they were dealing with choroideremia, choroidal sclerosis, or neither. The cases of Jacobson and Stephens[8] oft cited as examples of choroidal sclerosis, were not pictorially documented.

The X-linked cases of Stankovic[9] are typical of choroidal sclerosis. Francois[2] reviewed the general subject of X-linked chorioretinal hereditary degenerations. He classified them under three general categories: choroideremia, choroidal sclerosis, and pigmentary retinopathy. The last disorder was sub-classified into four forms: X-linked recessive, X-linked dominant, intermediate X-linked, and incomplete X-linked. He also reviewed the first reported cases of choroidal sclerosis of Thompson,[10] accepting them as bona fide examples. He further stated that Sorsby had made personal communication with Franceschetti and concluded



Table

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*Clinical Associate Professor of Ophthalmology, University of Minnesota Hospitals, Minneapolis.

†Professor, Oral Pathology and Director, Human Genetics Clinic, University of Minnesota Hospitals, Minneapolis.

that the cases he had reported with Savory[3] were actually examples of choroideremia. After considerable discussion, Francois[2] reached the conclusion that all X-linked forms of chorioretinal hereditary degenerations represented intermediate stages in the development of choroideremia.

We were prompted to write this communication based upon long observation of choroidal sclerosis in a large kindred that apparently has metamorphosed into choroideremia. This communication, thus, supports the observations of Krill and Archer[5] and Francois[2] that X-linked choroidal sclerosis represents a stage in the development of choroideremia.

The Table shows the pedigree of the family being reported. II-23 was the first member of the family examined. Examination was first carried out in 1958 when he was forty-four years old. Corrected vision at this time was 20/20 minus 1 and JO fairly well read, right eye, and light projection, left eye. At this time, he had a typical picture of marked choroidal sclerosis in both eyes. Both the posterior poles and mid-peripheries showed the exaggerated whitish choroidal vessels associated with both pigment accumulation and scattering and associated atrophy. Figure 1 shows the right eye at this time. On the first examination the left macula was involved with the whitish gray glial material.

Through the years there has been change in the fundus picture of both eyes so that when last seen in 1972, there was almost total involvement of the entire retina and choroid in both eyes. Figure 2 shows a fundus photograph, right eye, taken in 1971 wherein changes of both choroidal sclerosis and choroideremia may be seen in the same field. There was still evidence of a choroidal pattern of whitish vessels as seen with choroidal sclerosis, but there were also widespread areas in which there is simply a whitish background without choroidal pattern of vessels typical of choroideremia.

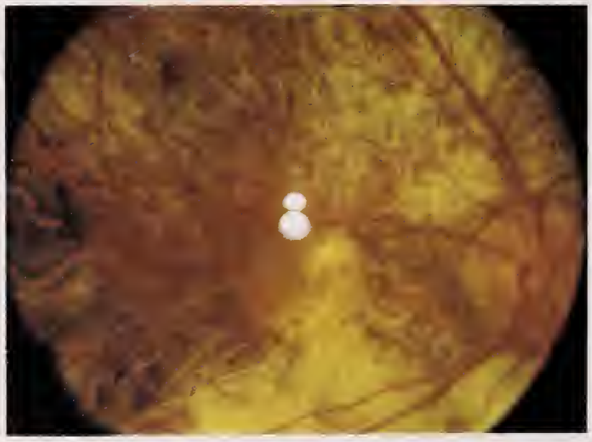

Fig. 1—II-23—Right eye—1958. "Choroidal Sclerosis." Exaggerated whitish choroidal vessels. Pigment accumulation, scattered atrophy.

Figure 3 is from the left eye taken in 1971

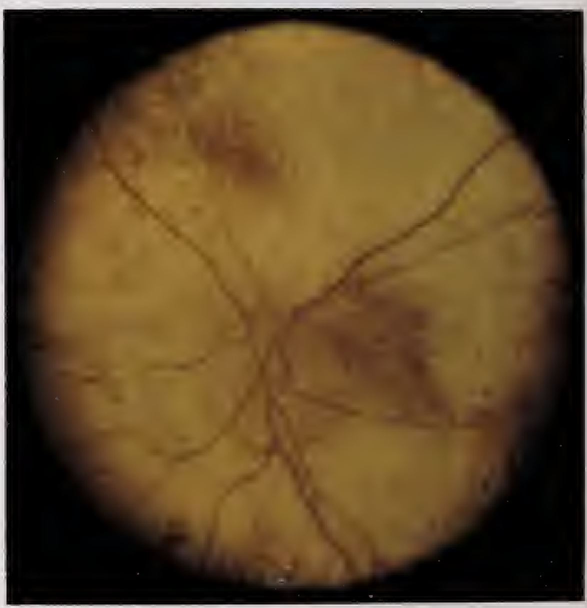

Fig. 2—II-23—Right eye—1971. "Choroidal sclerosis and choroideremia". Whitish choroidal vessels and widespread whitish background without vessels.

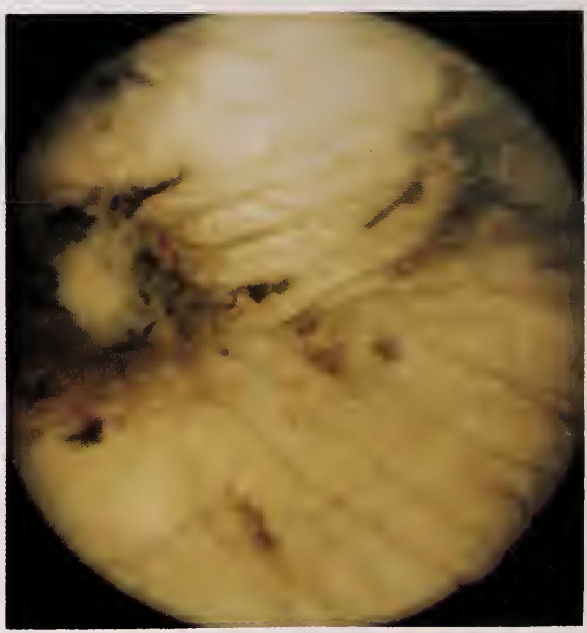

Fig. 3—II-23—Left eye—1971. "Choroideremia". No recognizable choroidal pattern. Marked atrophy, pigment accumulations.

showing essentially the picture of choroideremia wherein there is no recognizable choroidal pattern, marked atrophy, and pigment accumulations.

When first examined in 1958, the visual fields could be plotted, right eye, to a 2 White object at 1000 mm. and showed depression varying in that year between 5 and 15 degrees of field. No reliable field could be plotted, left eye. Visual fields taken in 1972 indicated no reliable field, left eye, and the visual field in the right eye had decreased to less than 5 degrees as plotted with a 45 white object at 1000 mm.

IV-53 is a four and a half-year-old male whose situation appears to be normal. There was some question of increased choroidal vessel prominence in the mid-periphery but this could not be defined as a definite abnormality and otherwise the fundi were normal. IV-62, his brother, two and a half-years-old, showed marked changes bilaterally in the retinal mid-periphery. The entire mid-periphery had significant increase in clumping of pigment granules and exposure of the choroidal cir-

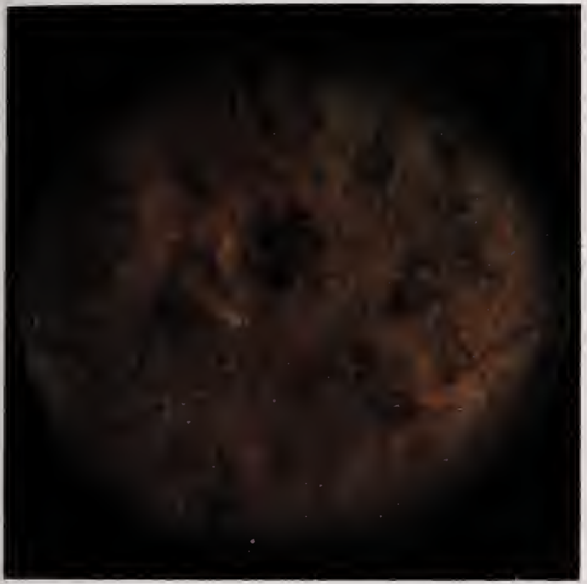

Fig. 4—III-53—1973. Female heterozygote—"Choroidal sclerosis" or "Choroideremia".—Mid peripheral pigment clumps.

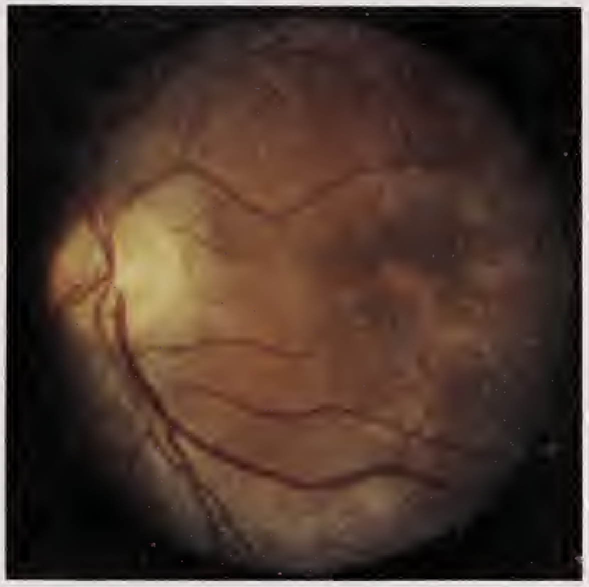

Fig. 5—III-53-1973. Female heterozygote—Macula and perimacula—slight orange tinge and fine disturbance of pigmentation.

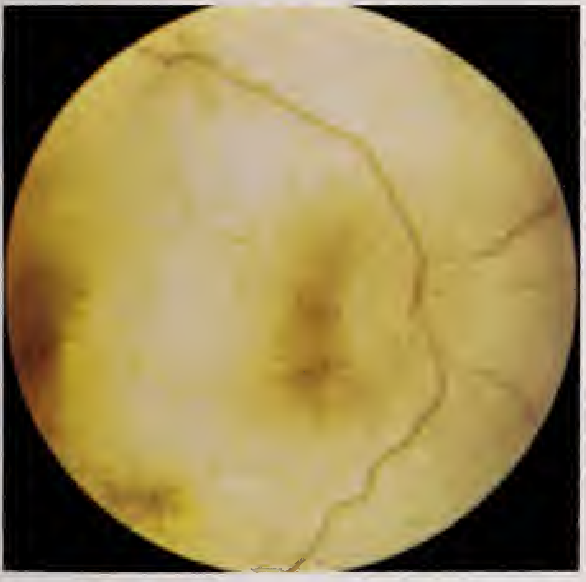

Fig. 6—II-25—Right eye—1973. "Choroideremia"—Some patches of reddish retina, otherwise essentially a white fundus.

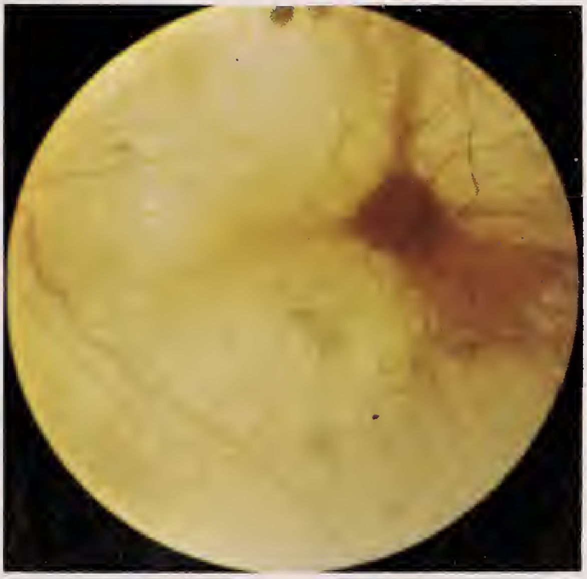

Fig. 7—II-25—Left eye—1973. "Choroideremia"—some patches of reddish retina—otherwise essentially a white fundus.

culation.

Their mother, III-55, exhibited definite fundus abnormality despite normal vision and visual fields. In the mid-periphery of her fundi were clumped pigment accumulations with some associated atrophy. There was also some exposure and exaggeration of the choroidal circulation.

III-53, despite normal vision and visual fields, had significant changes in her fundi. The mid-periphery showed granular pigment clumps and in addition in the macular and peri-macular areas, there was a slight orange tinge and a fine disturbance of pigmentation (Figures 4 and 5).

IV-61, her five-month-old daughter was difficult to examine but the posterior poles of the macular areas were normal. In the mid-periphery there was some suggestion of an exposed and exaggerated choroidal pattern. This probably represents an early carrier picture, but one cannot be sure.

II-24 currently married to II-23 was earlier epoused to II-25. Examination of II-25 showed no evidence of choroidal sclerosis or its carrier state. She had normal vision with glasses and normal visual fields.

II-13, sister of II-23, has clumped pigment accumulations in her mid-periphery, both eyes, with an area of atrophy infrotemporally in her right eye. Her choroidal vessels were not felt to be abnormal. Pigment changes were less dramatic than seen in some members. Her vision and fields were normal. Her daughter, III-39, had normal vision and visual fields, but there was some pigment granularity in the mid-periphery as in her cousin, III-43, but not nearly as marked as in her cousin, III-53. III-43 was examined only once in 1954 when she was 11-year-old and at that time her mid- and far-periphery showed only minimal granularity.

II-25, age 56, was examined in 1973, with a history that night vision had been decreased for twenty or twenty-five years. Vision was light projection, right eye, 20/25 minus, left eye. Visual fields were not plottable, right eye, and were markedly depressed, left eye. The right fundus showed a little reddish retina in the macular area, a few slightly reddish areas around the inferior vortex veins and occasional areas in the periphery showed exaggerated choroidal pattern but the rest of the fundus was white. There was a most interesting additional finding that supertemporally there was retinoschisis.

The left fundus showed some exaggerated choroidal circulation peripherally, occasional reddish spots of peripheral retina, a reddish area in the macular area and, again, almost a totally white fundus otherwise. A large retinoschisis was seen temporally (Figures 6 and 7).

Discussion

This report is thus the report of a family in which members in four generations have been observed. In a two and a half-year-old male, marked pigmentary disturbance in the fundus typical of choroidal sclerosis has been noted. In several generations of females, definite carrier states consistent with those described for choroidal sclerosis and choroideremia have been seen and in two males, both in their fifties, a current picture consistent with choroideremia is present. One of the individuals has been followed from 1958 to 1973, and presented initially with a fundus picture of choroidal sclerosis. This has evolved into a picture consistent with choroideremia still with persistent patches of choroidal sclerosis. The other seriously affected male examined presents predominantly as choroideremia with occasional residual evidences of choroidal sclerosis and the additional finding of bilateral retinoschisis.

The electrophysiologic data which could help confirm the diagnosis of choroideremia are not available in this pedigree.

This pedigree clinically supports the thesis that X-linked choroidal sclerosis is a stage of choroideremia.

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Mastoid Ecchymosis

Battle's Sign of Basal Skull Fracture

MILTON ALTER, M.D., Ph.D.;* PAUL STEIGLER, B.A. and MARY HARSHE, M.Ed.

A patient with mastoid ecchymosis associated with basal skull fracture was observed at the Veterans Hospital and illustrated Battle's sign.

Though heavily dependent upon laboratory studies in making a diagnosis, the modern clinician can still glean much from a careful bedside examination of the patient. In an earlier era (but not really so long ago), professional meetings included many reports on clinical signs and physicians unabashedly described their bedside observations without recourse to sophisticated laboratory tests. At such a meeting of the Royal College of Surgeons of England in 1890, William Henry Battle[1] described a sign observed in patients who had suffered a fracture of the base of the skull. He reported extravasated blood in the mastoid region after injury to the head. Though now known as "Battle's sign," Battle himself gave credit to Sir Prescott Hewett for recognizing the sign. Hewett (quoted by Holmes as cited by Battle[1]) wrote:

> "extravasation of blood, and consequent discoloration of the skin, appearing in the mastoid region some hours after a severe injury to the head, may lead to the suspicion of a fracture involving the posterior part of the base; and all the more valuable will this sign become if the injury did not bear directly upon this region, and especially if it bore upon the opposite side of the head."

Battle referred to the condition as

> "mastoid ecchymosis. That it appears in the first place in front of the apex of the mastoid process. That it often spreads upward over the mastoid in a line, slightly curved, and with the convexity backwards, its direction being approximately that of the outline of the external ear, from which it is distant half to three-quarters of an inch. At the end of three or four days after its appearance it diffuses itself forwards and backwards, chiefly in the latter direction, is most marked in the original line, and then gradually disappears. That it usually shows from the third to the fourth day after the injury, but its appearance may be delayed until the twelfth or fourteenth day. If the injury which is in the occipital region is to the right of the middle line, the ecchymosis will appear on that side over the anterior part of the apex of the mastoid process. That it may be accompanied with oedema and tenderness over the process. That the duration of the time which elapses between receipt of the injury and the appearance of the extravasation is to some extent an indication of the distance of the fracture from the process, the blood being compelled to travel by a certain anatomical route in order to reach the surface. That unless search be made for the extravasation, it is very apt to be overlooked, as the ear conceals it, especially if the ear is large and the head of the patient has not been shaved. Should the fracture have taken place in the middle line of the occipital bone, or should there be two or more lines of fracture diverging towards the foramen magnum from a point in the middle line the extravasation may appear on both sides and at a varying interval."

An attempt was made to provide an anatomical explanation for the mastoid ecchymosis after basal skull fracture. Dissections in cadavers, postmortem studies and experimental injections in humans of Berlin blue dye, glycerine and water were directed toward the foramen magnum. These studies showed that the muscles and fascia of the posterior neck and occiput effectively prevented direct passage of the extravasated blood from the site of the basilar skull fracture to the surface. Rather, passage was thought to occur between layers of the deep cervical fascia along a path created by the posterior auricular artery and aided along this path by the pumping action of the vessel's pulsations.

In 17 cases, Battle recorded the time when the mastoid ecchymosis was first perceived. The times varied from three to twelve days. Thus, the sign may not appear immediately and may be of little help if the patient is seen immediately after the injury. When it is seen, it may encourage the clinician to revise his prognosis or it may help account for a slower than expected recovery from head injury. It may suggest the need for additional x-ray studies of the skull with special attention to the base.

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See editorial, page 291.

In a survey of 2,684 cases of all types of skull fractures,[2] Battle's sign was reported in 52 (1.9%). Among the 52 cases, 15 died (29% mortality). Hence, its presence is not to be taken lightly. In an analysis of 432 of his own cases of skull fracture, Mock[2] observed 35 with Battle's sign (8%). The frequency with which Battle's sign is seen is dependent in part upon the diligence with which it is sought.

A patient with mastoid ecchymosis associated with basal skull fracture was observed at the Minneapolis Veterans Administration Hospital and afforded an opportunity to illustrate this valuable clinical sign.

Case Report

A 64-year-old male was admitted to the Minneapolis Veterans Hospital on May 18, 1972. He was involved

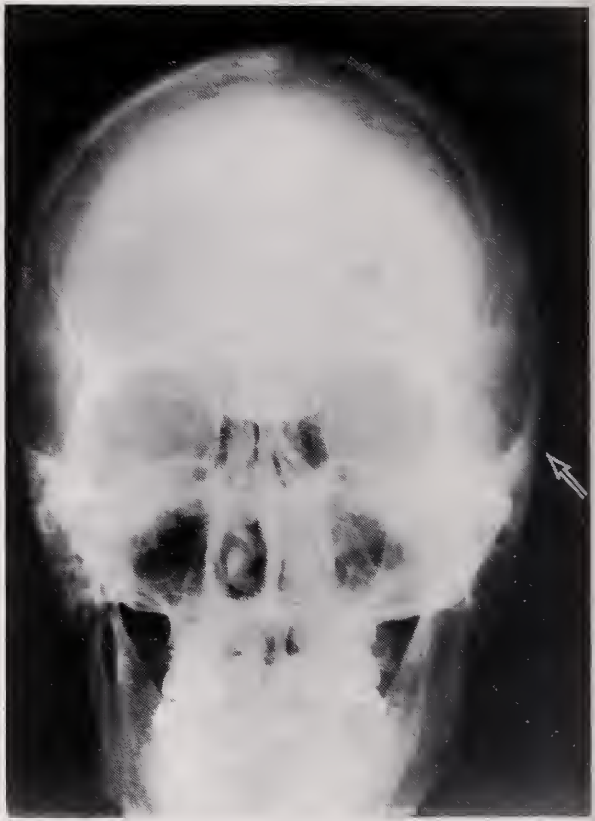

Fig. 2—Skull Xray showing basal skull fracture.

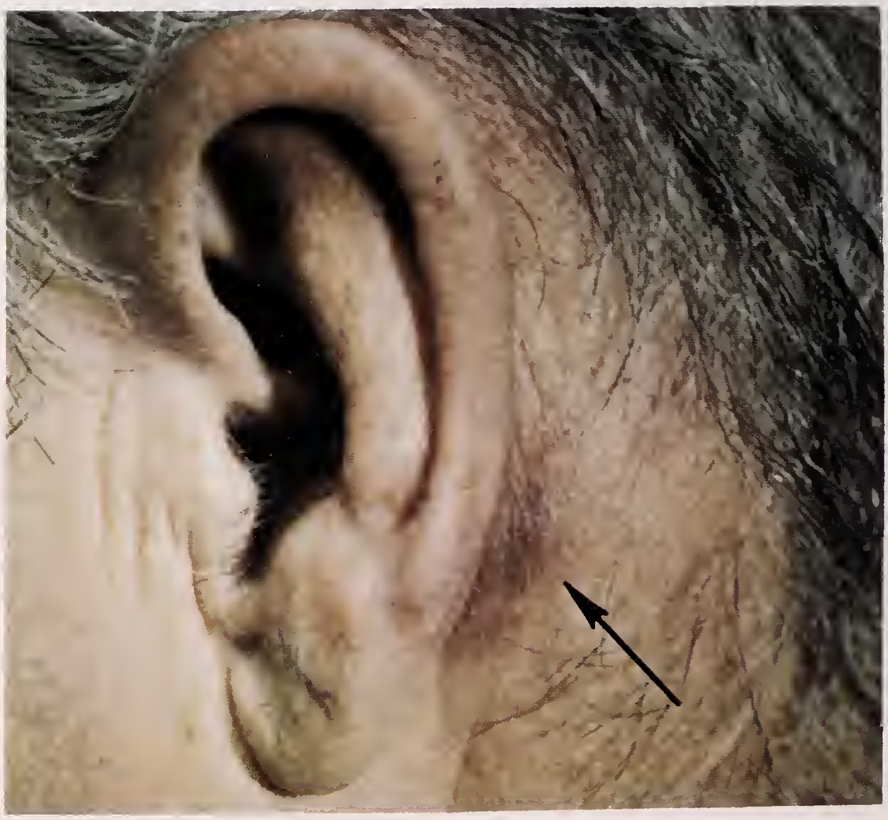

Fig. 1—Battle's sign (arrow).

in an automobile accident in April. He had amnesia for the details of the accident but recalled seeing a train and then he apparently hit it. He complained of headaches as well as back pain. There was some difficulty with memory. He had a previous accident in 1967 which caused a head injury but he apparently had no residual. A right thoracoplasty had been done in 1949.

On physical examination he was mentally slow and somewhat withdrawn with well-healed scars on the right and left side of the head. A Battle's sign was present on the left (Figure 1). There was a hemotympanum with decreased hearing on the left.

Laboratory studies were normal except for six to 10 white cells and occasional red cells on urinalysis. The EEG showed bilateral non-focal abnormalities. The skull Xray showed a fracture through the base (Figure 2). Lumbar and dorsal spine films showed minimal compression fracture of D11 & L2 with no loss of vertebral height. X-ray evidence of an old clavicular fracture on the right was seen and an acute fracture of the seventh rib was seen. Cervical spine films appeared normal. Brain scan was normal. Psychometric tests showed decreased mentation. He was discharged improved but mental function remained decreased.

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There is no such golden walk to Fortune as through the bowels of the credulous; and when sick, all men are credulous. Pain is a great leveler, alike hurling down sceptism, philosophy, and mere prosaic common-sense. The man, who before his friends will sneer at a vaunted specific—will sneak out by himself to seek the quack vendor of the despised anodyne.*

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*"Punch's Letters to His Son V. The advantages of being 'nothing'," Punch, 1843.

Painful Hepatic and Perihepatic Syndromes

In addition to the dull, continuous pain of chronic passive congestion of the liver during myocardial insufficiency, more acute episodes of pain may occur from involvement of other organs, according to Solervicens (Abst.). If there is a temporary insufficiency of the right ventricle, paroxysms of pain resembling an acute colic may appear in the right hypochondrium. This pain is said to occur particularly when the right ventricle empties its blood into a rigid, sclerotic lung that is incapable of handling or storing an increased amount of blood. It has also been pointed out that when cardiac insufficiency develops in the course of preexisting diseases of the liver, bile passages, stomach, or duodenum, this preceding disease may be aggravated and prolonged. Solervicens stated that when insufficiency of the right ventricle occurs in the presence of hepatic cirrhosis and pulmonary sclerosis an acute or subacute dilatation of the stomach and duodenum may be observed. He suggested that diseases of the liver may cause cardiac insufficiency in patients whose cardiac reserve is small or may intensify an already existing cardiac insufficiency.

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Problems in Pathologic Fractures

FRANKLIN H. SIM, M.D.*; ROBERT L. KRUSE, M.D.† AND
EINER W. JOHNSON, JR., M.D.‡

Although problems remain in the management of pathologic fractures, the application of newer techniques has resulted in much improvement. A high index of suspicion must be maintained when minor trauma results in a fracture. An adequate biopsy must be obtained in order to make a definite diagnosis. Internal fixation of a pathologic fracture has greatly benefited the patient. We have been pleased by the stability of the fixation when methyl methacrylate is used adjunctively with an internal fixation device. With this technique, the patient should not be denied the benefits of internal fixation even though the bone destruction is extensive.

PATHOLOGIC FRACTURES may be defined as fractures that occur through abnormal bone.[1] The structure and integrity of the bone may be so compromised that a pathologic fracture can occur with many different conditions. These have been classified by Coley and Sharp.[2] A pathologic fracture can be the first sign of a primary or a secondary bone tumor. Bickel and Barber,[3] in an analysis of more than 900 cases of pathologic fractures at the Mayo Clinic, found that 44% were due to metastatic disease, 41% to benign conditions, and 15% to primary malignant bone tumors. As in neoplastic disease, cortical weakness with subsequent pathologic fracture occasionally occurs in metabolic bone disease and in infective processes including tuberculosis, syphilis, and pyogenic osteomyelitis.

Benign Bone Tumors

Case 1

The patient was seen one month postpartum after fracturing her right femur by falling on the ice (Figure 1*A*). During the seventh month of her pregnancy, she had experienced a persistent aching discomfort in the right knee that worsened after delivery. Her hospital course had been complicated by intermittent fever that was attributed to endometritis. Results of laboratory investigation, including levels of calcium, phosphorus and alkaline phosphatase and protein electrophoresis, were within normal limits. Open biopsy revealed a typical giant-cell tumor. This was excised; the defect was packed with autogenous iliac bone chips, and stability was afforded by the Roger Anderson apparatus incorporated in plaster (Figures 1 *B* and *C*).

Comment

This case illustrates the importance of obtaining a good history because symptoms referable to the disease usually antedate the pathologic fracture. Recognition of a pathologic fracture is usually easy if a careful history is taken and if the roentgenogram shows a typically transverse, minimally displaced fracture with evidence of local bone destruction. However, one must maintain a high index of suspicion. Linscheid and Coventry[4] noted that an unrecognized stress fracture or an ossifying subperiosteal hematoma may mimic a malignant bone tumor.

This case also illustrates that diagnosis of the underlying cause of the pathologic fracture is often difficult and that confirmation requires an adequate biopsy and a microscopic study. Location of this tumor in the diaphysis was not suggestive of a giant-cell tumor, although two other such lesions in the Mayo Clinic series similarly spared the epiphyses.[5] The specific treatment of pathologic fractures depends on the underlying disease. In this case, treatment of both the giant-cell tumor and the complicating fracture required attention (Figure 1 *D*).

Fractures through a unicameral bone cyst occur in as many as 70% of patients. With conservative treatment of the fracture, the cyst can be treated best, after the fracture has healed, by curettage and bone grafting, although surgical treatment, if possible, should be delayed until the cyst has grown away from the epiphysis. Garceau and Gregory[6] stated that only 15% of the unicameral

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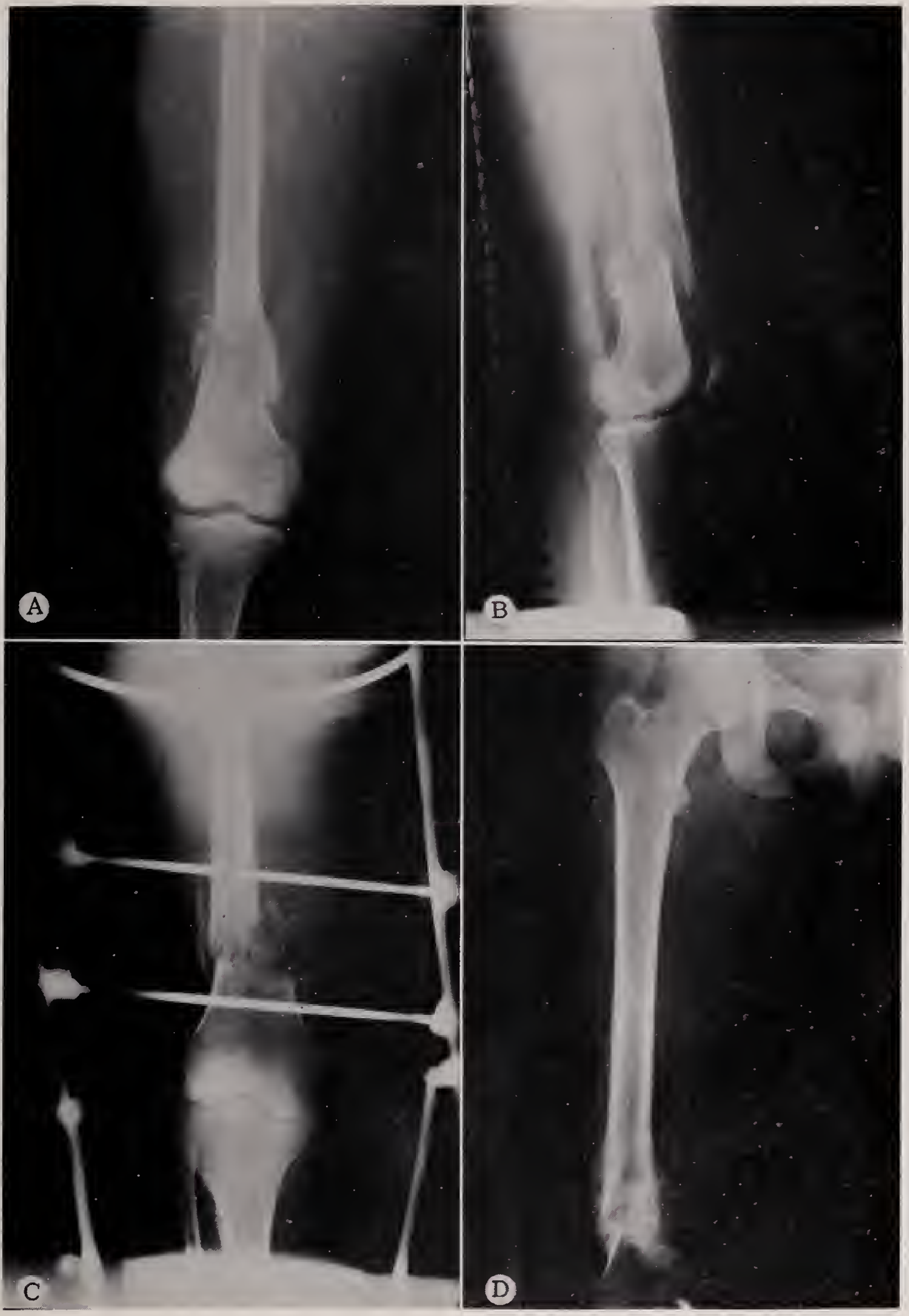

Fig. 1 (Case 1)—*(A)* and *(B)*. Right femur. Permeative lytic destructive lesion is present in distal femur, with pathologic fracture. Minimal displacement is apparent. *(C)* Distal femur. Lesion has been excised, and femur reconstructed with iliac bone grafts. Stability is afforded with multiple-pin fixation and Roger Anderson apparatus. *(D)* Distal femur seven months after surgery. Effective skeletal reconstruction has been achieved, with no recurrence of tumor.

cysts associated with a pathologic fracture heal spontaneously.

Malignant Bone Tumors

Case 2

A 52-year-old man noted a snap in his left arm as he reached to grasp a small object. Roentgenograms revealed a fracture that subsequently united in a hanging arm cast (Figure 2 *A*). When he was seen at the Mayo Clinic five months later, with recurrent pain, the roentgenogram (Figure 2 *B*) revealed an underlying pathologic process. Open biopsy confirmed multiple myeloma.

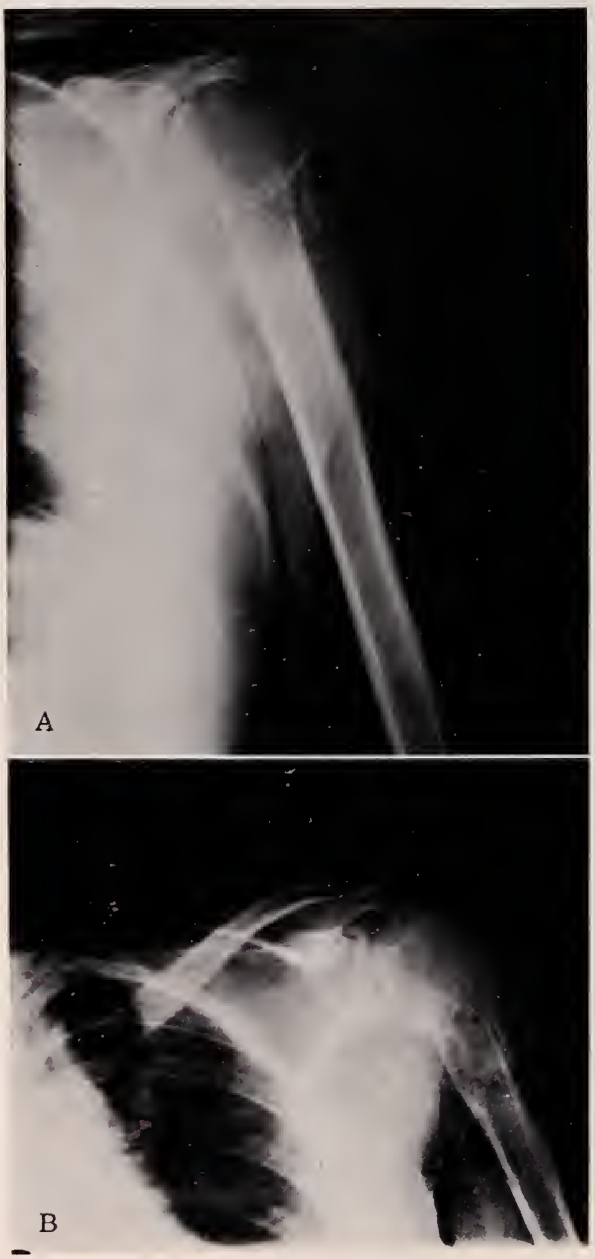

Fig. 2 (Case 2)—*(A)* Left shoulder. Fracture of proximal humerus. Destructive changes are distorted by fracture fragment. *(B)* Pathologic fracture has united five months later; however, underlying pathologic destructive changes are apparent.

Comment

This case illustrates the importance of having a high index of suspicion when a trivial injury causes a fracture and the importance of knowing that the normal roentgenographic characteristics of the lesion are distorted by the fracture, thus making interpretating the roentgenograms difficult. Pathologic fractures in an osteogenic sarcoma have been reported to shorten life expectancy.[2] In pathologic fracture of an extremity associated with a sarcoma, the extremity must be amputated before systemic dissemination occurs. Prompt ablative surgery offers the best choice for cure—a cure reported at approximately 20% in most large series.[5]

Metastatic Bone Disease

Case 3

A 61-year-old housewife with a hypernephroma underwent right nephrectomy in September 1968. She was seen at our clinic four years later because of severe pain and inability to move her right arm. Examination revealed a pathologic fracture of the sixth rib, with extensive destruction of the midshaft of her right humerus and an imminent pathologic fracture (Figure 3 *A*). Prophylactic internal fixation was carried out, and excellent stability was achieved by the use of a Rush rod combined with methyl methacrylate. Pain was relieved,

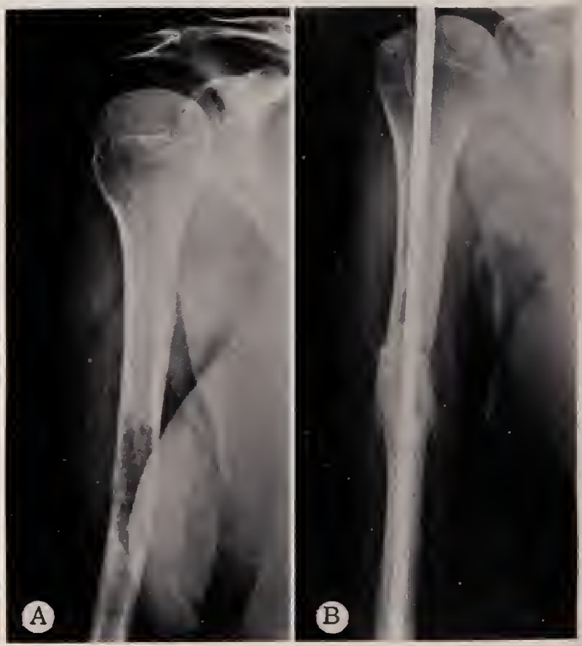

Fig. 3 (Case 3)—*(A)* Metastatic hypernephroma of midshaft of right humerus, with extensive osseous destruction and imminent pathologic fracture. *(B)* Right humerus. Excellent stability has been achieved by the use of methyl methacrylate and intramedullary rod.

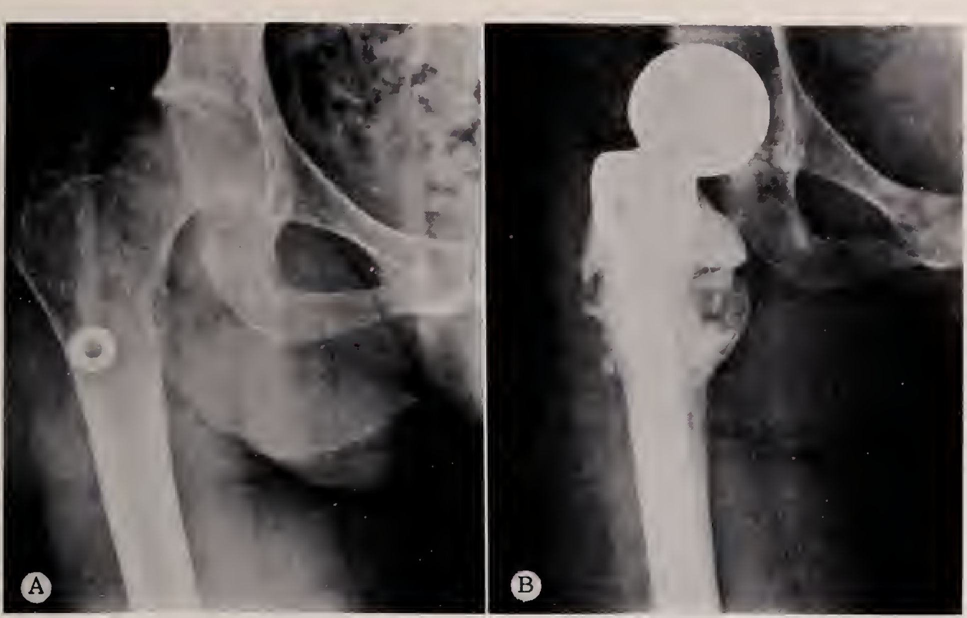

Fig. 4 (Case 4)—*(A)* Right hip. Extensive osseous destruction of proximal femur, with metastatic breast carcinoma. Pathologic subcapital fracture. *(B)* Right hip after prosthetic replacement. Integrity of destroyed calcar and lateral cortex has been restored by the use of methyl methacrylate.

and excellent function was restored (Figure 3 *B*). She died of her disease eight months later.

Case 4

A 37-year-old woman underwent radical mastectomy for cancer of the breast in May 1969. She was seen at the Mayo Clinic in March 1971 with a five-month history of right hip pain. She became disabled with a great deal of pain after a minor fall several days prior to admission. Roentgenograms revealed extensive destruction of the left hip extending below the lesser trochanter, with a pathologic subcapital fracture of the calcar and lateral cortex (Figure 4 *A*). The local factors of tumor destruction necessitated the use of a femoral head and neck prosthesis held firmly in place with methyl methacrylate (Figure 4 *B*). After the surgery, she could walk independently with the aid of a cane, and when seen one year later, she was active.

Comment

The most common pathologic fracture is through an area of metastatic disease,[3] and this unfortunate complication commonly leads to a painful downhill course, the patient being bedridden with pneumonia and decubitus ulcers. The application of basic principles of fracture treatment with internal fixation makes it possible for the patient to walk; the pain can be relieved with proper fixation, and the prolonged confinement with its complications can be prevented.[7] It is easier to prevent pathologic fractures than to treat them, and prevention decreases the morbidity greatly and makes it easier to treat the tumor. Recent improvements in joint replacement techniques make it possible to restore function in joints destroyed by a neoplastic process.

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*Lord! methought what pain it was to drown!**

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*Shakespeare: Richard III. I.iv.21. c. 1593.

Penetrating Thoracic Trauma

The Basic Principles of Surgical Wound Treatment[*]

RAYMOND C. BONNABEAU, JR., M.D.[†]

The basic concepts in the operative management of penetrating thoracic injuries have been reviewed by means of illustrative cases. These include conservative management (wound debridement, tube thoracotomy); operative management through the extended "wound thoracotomy," and definitive operative treatment by means of formal thoracotomy.

THORACIC INJURIES have formed about eight per cent of all military injuries in modern warfare.[1] With the increasing use of the automobile as a principal method of travel in this country, the

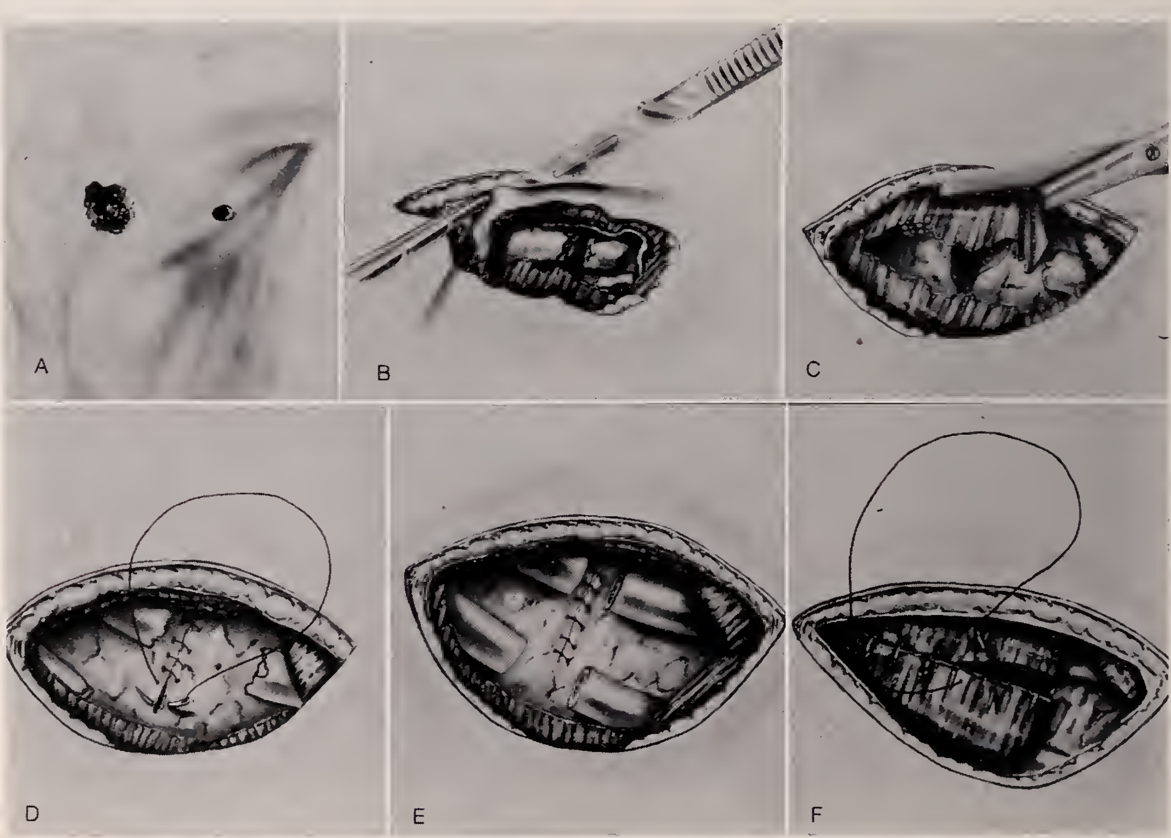

Fig. 1—(A) Drawing of the chest in a 23-year-old male who sustained a high velocity gunshot wound of the right chest which entered below the right axilla and exited beneath the scapula. He was treated in a conservative manner (wound debridement and tube thoracotomy). At debridement (B), small amounts of damaged skin and larger amounts of contused, non-viable muscle (C) and bone spicules were removed. The underlying lung was sutured because of continued bleeding (D). The jagged edges of the ribs were trimmed to prevent further pulmonary laceration (E) and the wound made airtight by suturing together the overlying musculature (F).

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treatment of thoracic trauma is now of prime concern to the civilian physician as well as his military colleague. While the military and civilian causes of the trauma are different, the basic principles of surgical wound management are essentially the same.

This paper attempts to review briefly the basic principles of surgical management in penetrating wounds of the thoracic cavity by means of illustrative clinical examples.

Categories of Surgical Wound Management

Operative management of penetrating wounds of the thoracic cavity fall into three broad categories: (1) Conservative operative management; (2) operative management by means of the extended "wound thoracotomy;" (3) operative management by means of formal thoracotomy.

Conservative Operative Management: Tube Thoracotomy and Wound Debridement.

Case Reports

Case 1

A 23-year-old male accidentally sustained a through-and-through gunshot wound (muzzle velocity 2500 feet per second) of the right chest wall at relatively close range. A small entrance wound was present in the anterior right axilla and a large wound of exit was below the right scapula (Figure 1A). An occlusive dressing of vaseline gauze and tape had been placed prior to his admission to the West Virginia University Hospital. Initial chest Xray (Figure 2A) revealed a moderately contused right lung and a hemopneumothorax. Initial treatment consisted of tube thoracotomy with a large bore (#36 French) chest catheter* attached to an Emerson suction.† This evacuated the air and approximately one unit of blood. The patient was then taken to the operating room where under general anesthesia wound debridement was carried out (Figures 1B and 1C). The exit wound in the pulmonary parenchyma itself necessitated primary suture because of bleeding (Figures 1D and 1E). The openings into the thoracic cavity were closed by mobilizing and suturing adjacent muscle flaps with chromic catgut (Figure 1F). The skin and subcutaneous tissues were left open and covered with a single layer of fine mesh gauze. Five days later these were loosely approximated by means of interrupted #2 nylon sutures (delayed primary closure). Chest Xray three months later showed some chronic changes (Figure 2B).

Case 2

A 15-year-old white male, was admitted to the West Virginia University Hospital after sustaining a 12-gauge shotgun blast at a range of five feet in the left upper chest. Chest Xray (Figure 3A) revealed three fractured ribs as well as destruction of the middle third of the clavicle and scapula. Severe pulmonary parenchymal contusion was present. This caused a moderate ventilation-perfusion defect which necessitated an endotracheal tube and respirator for 24 hours. After initial placement of a chest tube, the patient was taken to the operating room where extensive debridement was carried out. Miraculously, the major axillary vessels had been spared and only minor damage had occurred to the brachial plexus. The wound was loosely covered with fine mesh gauze to promote drainage. Five days later the patient was taken back to the operating room where under general anesthesia a delayed primary closure was carried out. Six months later, after complete healing, a chest

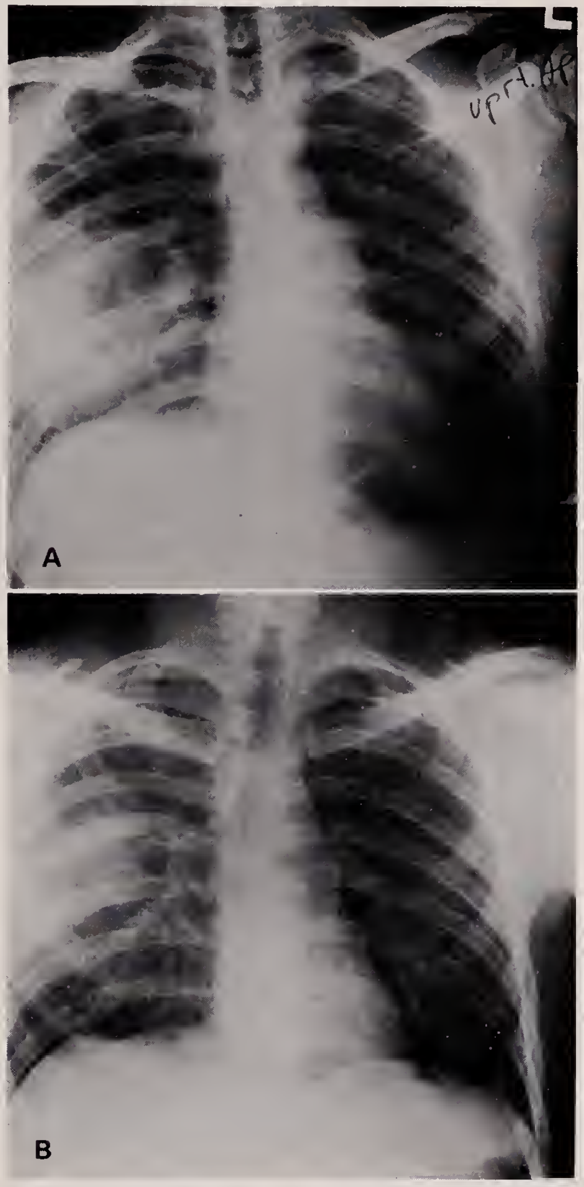

Fig. 2—(A) PA Chest Xray of a 23-year-old male (Figure 1) who sustained a high-powered gunshot wound of the right chest. A hemopneumothorax and a moderately severe degree of pulmonary contusion (the latter resulting in a mild ventilation-perfusion defect) were present. (B) PA chest Xray of the same patient taken approximately three months following discharge from the hospital. Some persistent chronic pulmonary changes can be seen. The patient had recovered completely.

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*Sherwood Medical Industries, Inc., St. Louis, Mo.

†J. H. Emerson Co., Cambridge, Mass.

Xray revealed normal aeration and expansion of the lung (Figure 3B).

Comment

It is fortunate that definitive management in the majority of penetrating thoracic injuries consists in the proper placement of a large bore chest catheter connected to water seal suction or drainage, together with wound debridement and closure. Multiple tube placement is usually necessary only in cases of incomplete pulmonary expansion or loculation of fluid or air. Correct placement of chest tubes in these cases can be facilitated by the use of fluoroscopy.

In thoracic trauma cases, chest tubes are best inserted along the patient's anterior axillary line, somewhat lateral to the nipple (Figure 4A). This places it away from vital structures and avoids the pectoral muscle mass. The latter facilitates insertion. Adequate infiltration with local anesthesia of the skin, muscle, rib periosteum, and parietal pleura is mandatory prior to catheter insertion. A suitable incision (at least large enough to admit the index finger of the operator, which is approximately the size of a #36 French chest catheter) is then made at the skin level. After insertion of the finger through this incision, a scalpel (or hemostat) can be placed under the fingertip and the muscular portion of the chest wall dissected alternately by means of blunt (fingertip) and/or sharp (scalpel blade or hemostat tip) dissection (Figure 4B). To help prevent air leaks, the line of dissection should be angled some distance from the skin to the parietal pleura.

The thoracic cavity should be entered *first* by the fingertip. This not only minimizes the danger of trauma, but limited exploration at that time can assure the operator that the general thoracic cavity, or the correct portion of the cavity (if a loculated area is to be drained) has indeed been entered and that a vital organ is not about to be damaged (Figure 4C).* The chest tube can then be grasped a short distance behind its rounded tip by a hemostat. This assures tube stability and tends to prevent the sharp tip of the clamp from entering the chest first and causing injury. The chest catheter can then be gently introduced as the operator's finger is withdrawn and finally sutured into place (Figure 4D).

The blind creation of a tunnel by "ramming" home a large hemostatic clamp can only be condemned.†

Debridement of open chest wounds (similar

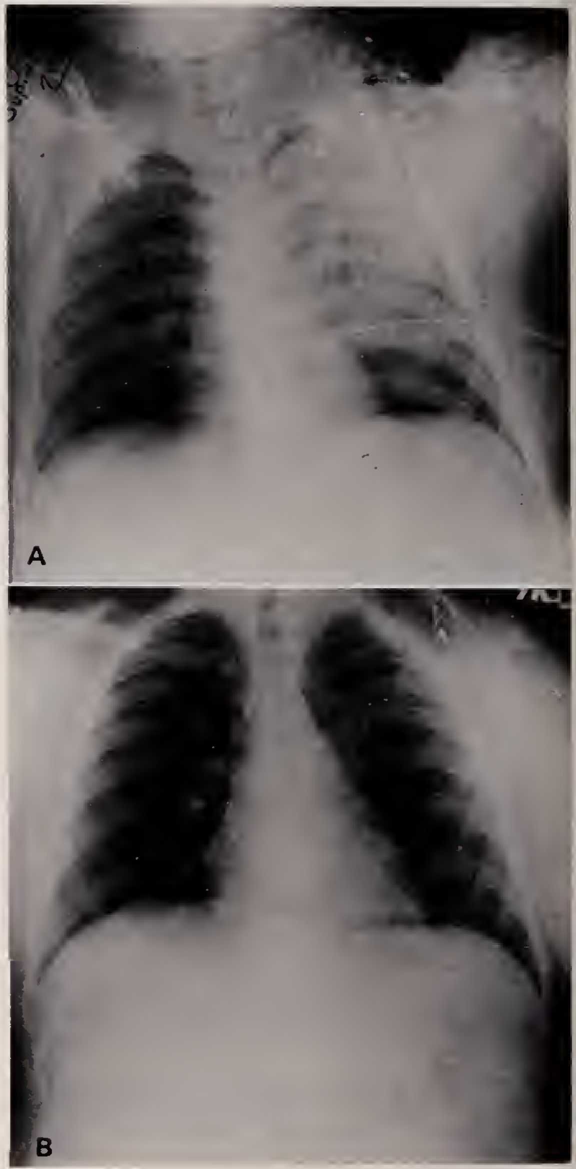

Fig. 3—(A) AP chest Xray of a 15-year-old patient who had sustained a 12-gauge shotgun blast (from five feet) to the upper portion of the left chest. The blast fractured three ribs and had carried off the middle third of the clavicle and upper third of the scapula. No major vessels or nerves were injured. Severe pulmonary parenchymal contusion which accounted for a moderate ventilation-perfusion defect was present. Operative treatment was conservative (wound debridement and tube thoracostomy). (B) PA chest Xray six months later. Complete expansion and healing of the left lung had occurred.

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*While needle aspiration of the thorax at the time of anesthetic infiltration may be helpful to determine one's location prior to tube insertion, it is not in my experience necessarily definitive in this regard.

†The author has seen two rather dramatic fatalities when these methods were used. The chest tube tunnels in each case were made by blindly ramming a hemostat into what was thought to be the thoracic cavity but was in fact the right lobe of the liver below the diaphragm.

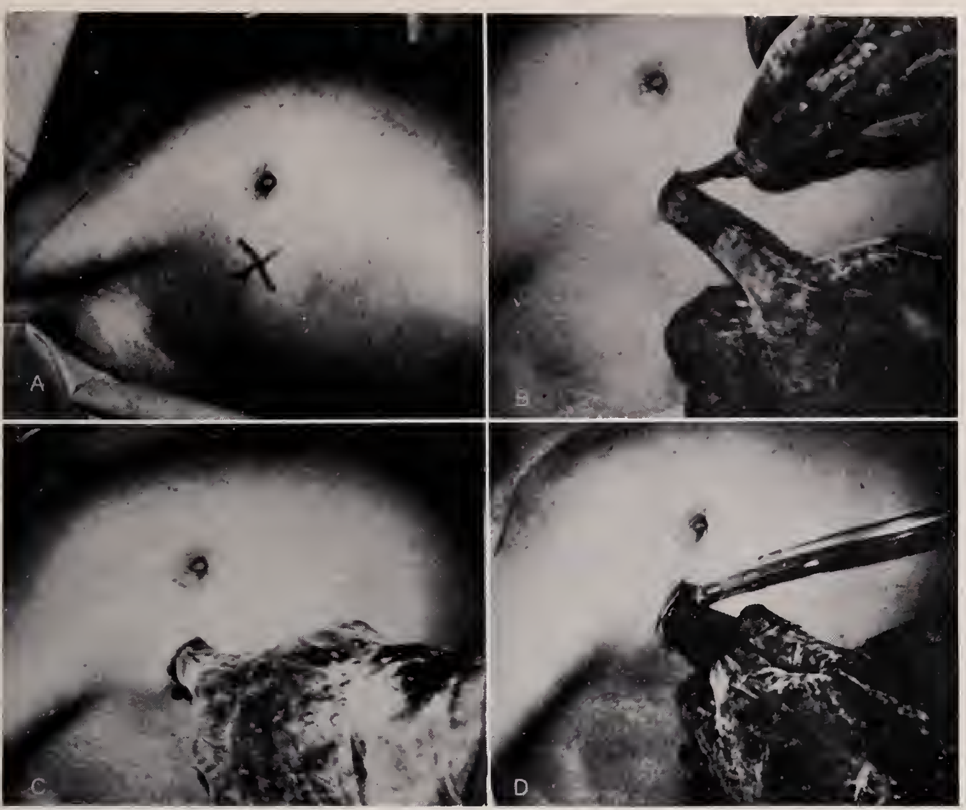

Fig. 4—Photographs illustrating the method of chest tube placement in patients with intrathoracic trauma. (A) The skin incision is best made in the anterior axillary line, lateral to the nipple (at the site marked). This avoids both the important thoracic structures and the large pectoral muscle mass. (B) Following a suitable skin incision, the index finger is inserted and a scalpel (shown here) or hemostat placed under the fingertip and the muscular portion of the chest wall dissected by alternate blunt (fingertip) and sharp (scalpel blade or hemostat tip) dissection. (C) The chest cavity should initially be entered by the exploring finger to minimize trauma. (D) The chest tube is then grasped by a hemostat (a short distance behind its rounded tip) and gently inserted as the exploring finger is removed.

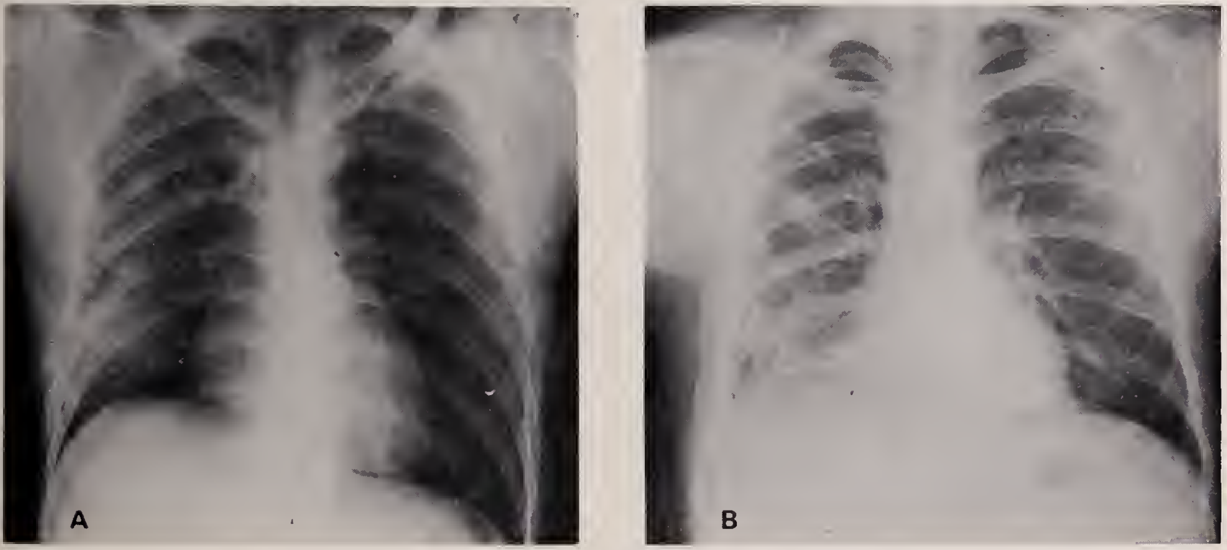

Fig. 5—(A) PA chest Xray of a 28-year-old male who had a stake driven into his right chest during an automobile accident, resulting in a significant chest wall defect. Because of the low velocity of the trauma, a minimal degree of pulmonary contusion was present. (B) Chest Xray of the same patient taken three months later. Some chronic pulmonary changes may be seen, but the lung was completely expanded and the chest wall healed (Figure 6).

to debridement anywhere) is carried out by resecting small amounts of damaged skin together with larger amounts of dead, contused, and compromised underlying muscle. All loose pieces of foreign debris and bone spicules should be removed, the wound irrigated, and the defect closed with overlying viable muscle. The skin and subcutaneous tissue can be left open and covered (not packed) with a single layer of fine mesh gauze to allow drainage for approximately five days, when a delayed primary closure can be carried out.

Although pulmonary parenchymal contusion did occur in the cases presented, this resulted in only mild ventilation-perfusion defects which were not of prolonged clinical significance. Massive pulmonary contusion can, however, result in a severely depressed arterial pO_2. This may not be significantly improved despite the use of a respirator and an FIO_2 of 100 per cent. In these cases, a satisfactory arterial pO_2 has been obtained only after resection of the damaged pulmonary parenchyma.[3,4,6]

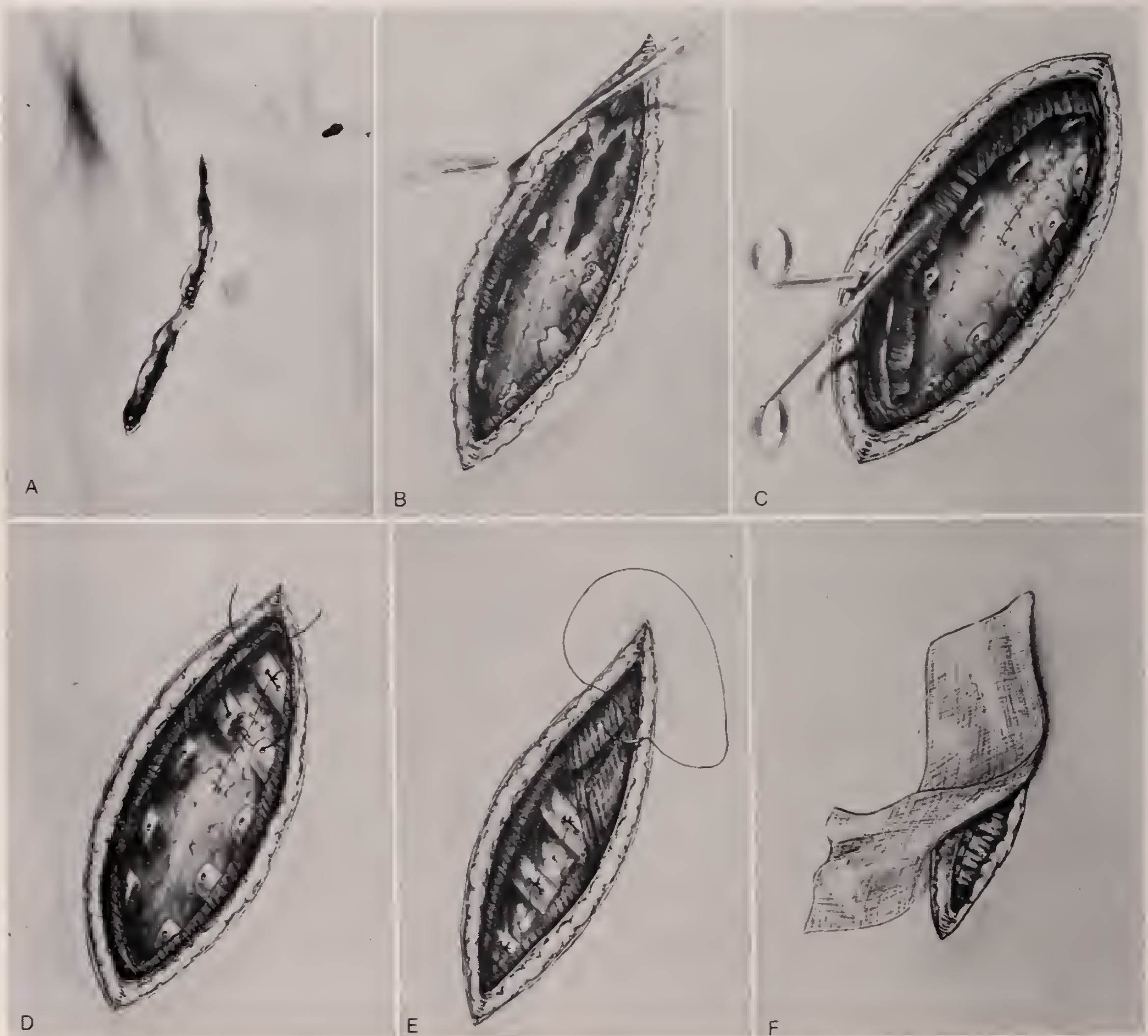

Fig. 6—Illustrative drawings depicting the treatment of a penetrating chest wound by means of an extended "wound thoracotomy" in a 28-year-old male who had a stake driven into his right chest during an automobile accident (see Xrays, Figure 5). (A) The chest wall defect extended from the clavicle to beneath the right axillary region. The jagged edges of five broken ribs had damaged the upper, middle, and lower lobes of the right lung. At operation, debridement of a small amount of skin (B), and a larger amount of contused underlying musculature (C) was undertaken. Widening of the incision allowed the ribs to be trimmed and holes drilled so their edges could be approximated to prevent further lung entrapment (D). Extension of the thoracotomy also allowed portions of the devitalized upper, middle, and lower lobes to be removed. The overlying defect was closed by mobilizing flaps of thoracic musculature (E). The wound was left open and covered with a single layer of fine mesh gauze (F), and closed five days later.

Extended "Wound Thoracotomy" Limited thoracotomy (incision extension of the wound edges), limited intrathoracic exploration, wound debridement, and tube thoracotomy.

Case 1

A 28-year-old male, was involved in an automobile accident, at which time a stake was driven into his right chest. This left a significant chest wall defect and five fractured ribs whose jagged edges had trapped (thus preventing a pneumothorax) and lacerated portions of the upper, middle, and lower lobes of the right lung. Initial treatment consisted in emergency suture of the skin defect to prevent air leakage. Because the chest damage had been sustained at a low velocity, minimal pulmonary contusion was present on chest Xray (Figure 5A).

After arriving at the West Virginia University Hospital, the patient was taken to the operating room where the external wound (Figure 6A) was explored and debrided, and the jagged rib edges smoothed. The wound was extended and the devitalized portions of the right lung were removed and the lung sutured (Figures 6B and 6C). In order to stabilize the chest wall and also to prevent further lung damage due to rib entrapment, drill holes were placed in the tips of the fractured ribs and their edges approximated by means of #2 nylon sutures passed through these holes (Figure 6D). The chest cavity was washed out with saline and three chest catheters were placed under direct vision. The defect in the chest wall was then made air tight by mobilizing large flaps of pectoral muscle and suturing them with #1 nylon (Figure 6E). The skin and subcutaneous tissue were then covered with a layer of fine mesh gauze (Figure 6F). The patient made an uneventful recovery. Three months later, some right sided pleural reaction was seen on Xray (Figure 5B).

Comment

The patient illustrates the need that arises in some patients for an extended thoracotomy (when wound position permits) to facilitate repair of more extensive intrathoracic damage. In this case, intrathoracic lavage and removal of a moderate amount of devitalized pulmonary tissue were necessary. Due to the nature of the defect, these maneuvers could be carried out without formal thoracotomy. Operative debridement with intrathoracic repair, lavage, and the proper placement of chest catheters with adequate lung expansion and thoracic drainage resulted in complete healing.

Formal thoracotomy occasionally may be necessary for a specific penetrating injury complication where definitive operative manipulation cannot be carried out by any other means.

Case 1

An ARVN* soldier was admitted to the 27th Surgical Hospital RVN† with multiple small fragment wounds of the right arm, chest, and abdomen. Examination of the Xrays and the condition of the patient initially seemed to indicate that a cardiac injury was present. The patient was taken to the operating room and ex-

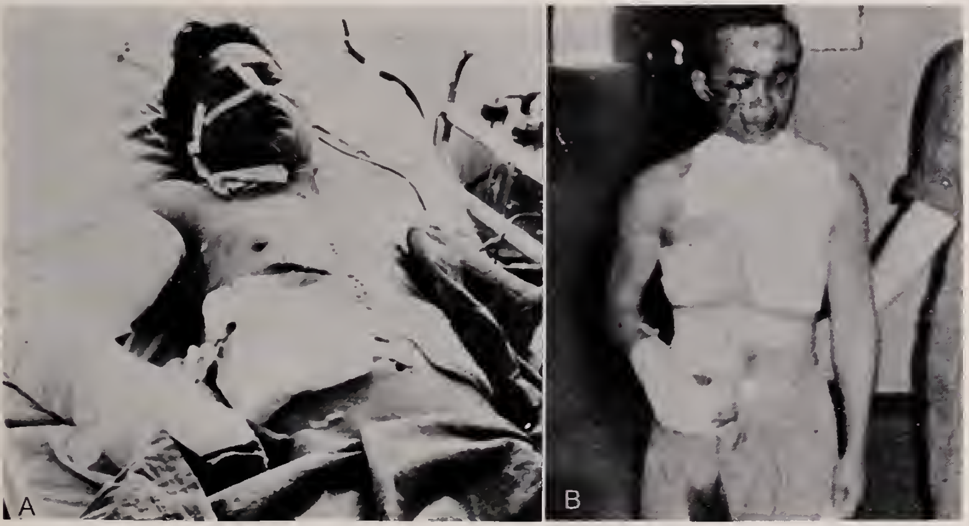

Fig. 7—(A) Photograph of an ARVN soldier, three days postoperatively, admitted initially with multiple fragment wounds of the chest and abdomen. The thoracic injuries and massive contusion of the liver were repaired through a thoracoabdominal approach (midline sternotomy continued into the abdomen). [See index for details.] (B) Photograph of an ARVN soldier one week postoperatively who sustained multiple fragment wounds of the head, chest, hand, and abdomen. Operation consisted of laparotomy for abdominal wounds and an emergency left thoracotomy for bleeding from a lacerated axillary vein and artery. Both of these cases are examples of penetrating wounds which necessitated formal thoracotomy.

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*Army Republic of Vietnam

†Republic of Vietnam

plored through a mid-sternotomy. This revealed a lacerated pericardium but an intact myocardium. Contusions of both lungs and several large penetrating wounds of the right and left hemidiaphragms with underlying liver damage were present. The thoracic wound was extended into the abdomen as a midline incision. Massive damage to both the left and right lobes of the liver, as well as a ruptured spleen, was present. The spleen was removed and the liver injuries sutured and widely drained. Multiple chest catheters (#36) were placed in the thoracic cavities and the long incision closed (Figure 7A). The patient had a stormy postoperative course, but was discharged to a Vietnamese hospital approximately two months later.

Case 2

An ARVN soldier was admitted to the 95th Evacuation Hospital RVN with multiple fragment wounds of the eye, head, chest, abdomen, and right hand. The patient's condition necessitated enucleation of one eye, amputation of the fingers of the right hand, and exploratory laparotomy. While debriding the left upper chest wound, a sudden, steady blood loss occurred and an emergency left anterior thoracotomy had to be carried out.* Bleeding came from a traumatic laceration of the axillary artery and vein. Both vessels were mobilized and ligated, and the chest closed and drained through #36 chest catheters. The patient did remarkably well and was sent to a Vietnamese army hospital several weeks later for prolonged care (Figure 7B).

Case 3

An ARVN soldier was admitted to the 95th Evacuation Hospital RVN with a gunshot wound of the left chest (small entrance wound below the tip of the left scapula, no exit wound). Chest Xray (Figure 8A) revealed an M-16 bullet in the mediastinum in the region of the right ventricle. A left hemopneumothorax had been cleared by means of a #36 chest catheter. Auscultation of the patient's chest revealed a metallic slapping sound that corresponded to the patient's cardiac cycle.

The patient was immediately taken to the operating room where the pericardium was opened through a mid-sternotomy and approximately 200 cc of blood aspirated. An M-16 bullet was found lying free in the pericardial sac (Figure 8B). This was removed and a small contused area of the left ventricle (penetrated by the tip of the bullet) sutured with several 2-0 silk sutures. The pericardium was loosely approximated with 00 chromic catgut and the mediastinum drained through the left pleura into the left chest, where a #36 chest tube was placed. The patient made an uneventful recovery. (Figure 8C).

Case 4

A 40-year-old white male, was accidentally shot in the anterior left chest and admitted to the West Virginia University Hospital. Chest Xray revealed a left-sided hemopneumothorax and a 22-gauge bullet lodged in his upper mediastinum in the region of the trachea and aorta (Figures 9A and 9B). Approximately 200 cc of blood and air were removed by means of tube thoracostomy. At bronchoscopy, a small contusion on the left lateral surface of the bronchus (where the bullet was lying on Xray) was found. There was no penetration. No mediastinal widening was present. Two days following his admission, an aortogram was performed (Figures 10A and 10B). The bullet was lying between the left carotid and subclavian arteries, immediately above and behind the aorta. All the vessels appeared undamaged. The esophagus was intact (Figure 10C).

Although our original plan involved leaving the bullet in place,† operative removal was considered necessary by all examining physicians after the patient became depressed and agitated when we were not able to guarantee him absolute freedom from future complications

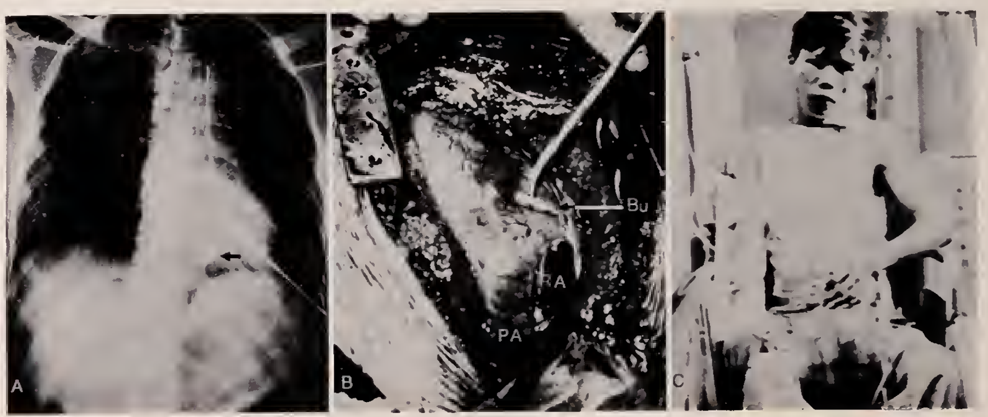

Fig. 8—(A) AP chest Xray of an ARVN soldier admitted with a gunshot wound of the left posterior chest. An M-16 bullet (arrow) may be seen in the region of the right ventricle. (B) Photograph taken during the subsequent thoracotomy (mid-sternotomy). The vantage point is that of the anesthesiologist. The M-16 bullet (Bu) was found lying free in the pericardium. A small lacerated area in the left ventricle had to be sutured. (RV-right ventricle, PA-pulmonary artery, RA-right atrium.) (C) Photograph of the patient two days postoperatively.

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*This patient was operated upon by LTC Richard Shaw with the author as assistant.

†There was a difference of opinion among thoracic surgery staff members who saw this patient at this time. Half felt operative removal was necessary and half felt the bullet should be left in place.

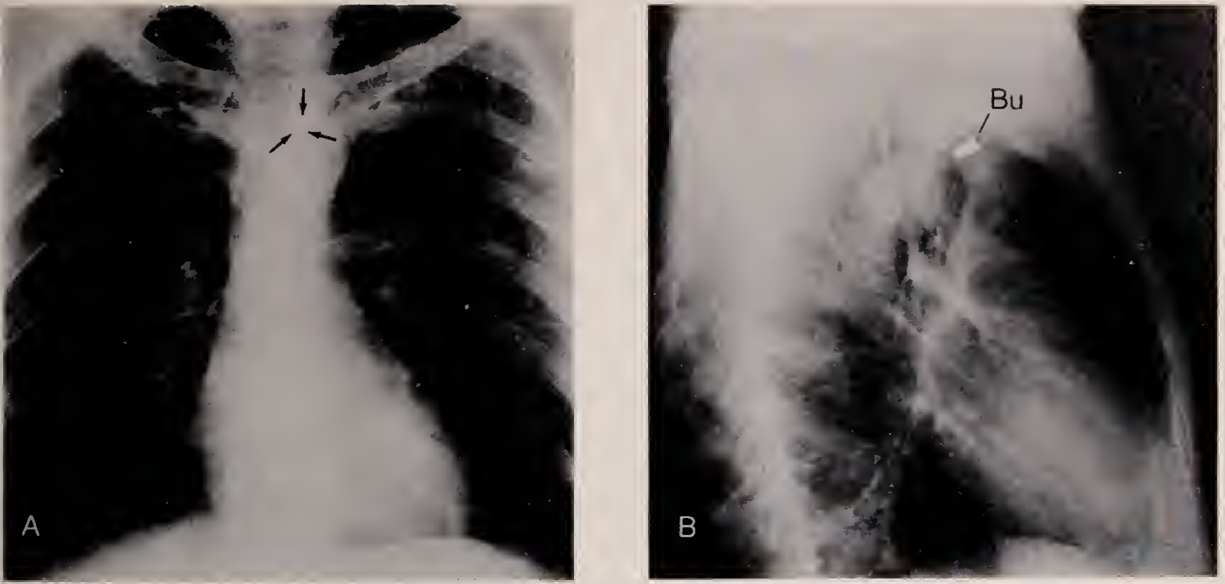

Fig. 9—(A,B) PA and lateral chest Xray of a 40-year-old male accidentally shot with a 22-caliber bullet in the left chest. The bullet (Bu, arrows) may be seen lying in the high mediastinum.

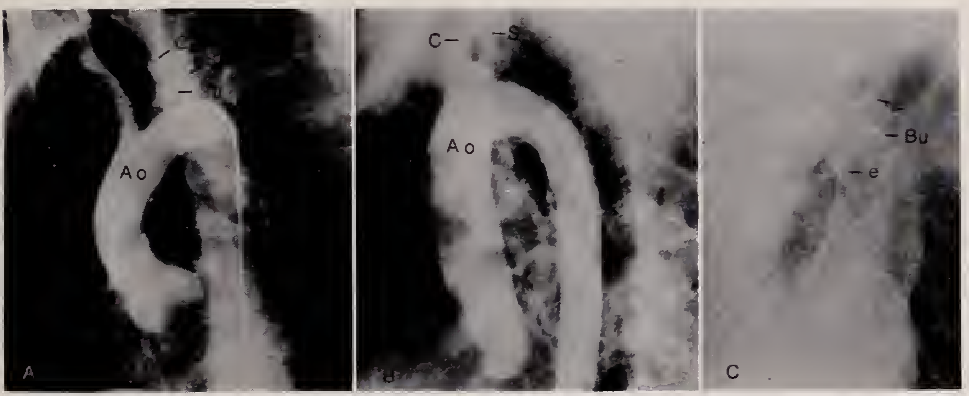

Fig. 10—(A,B) Aortogram obtained in the patient (Figures 9A, 9B and 11) with a 22-caliber gunshot wound in the left chest. The bullet (Bu) may be seen lying over the top of the aorta (Ao) between the left carotid (C) and subclavian (S) arteries. Bronchoscopy had revealed no penetration of the tracheal wall. (C) Esophagram showed the bullet (Bu) lying some distance from the esophagus (e).

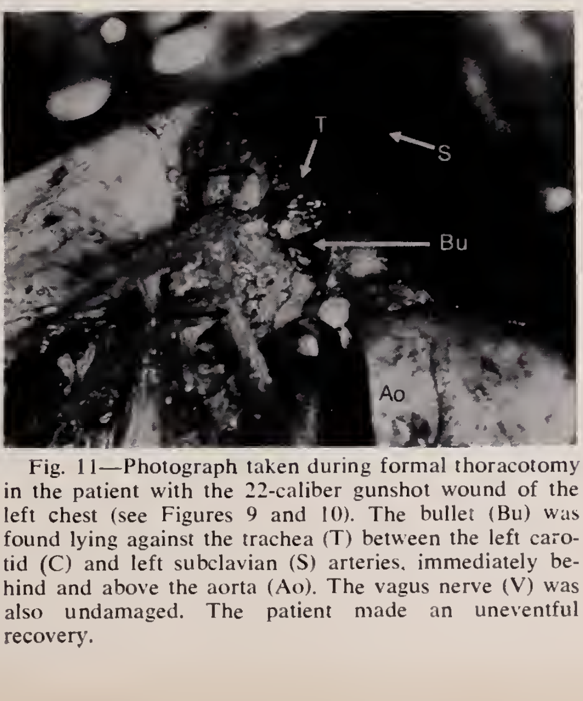

Fig. 11—Photograph taken during formal thoracotomy in the patient with the 22-caliber gunshot wound of the left chest (see Figures 9 and 10). The bullet (Bu) was found lying against the trachea (T) between the left carotid (C) and left subclavian (S) arteries, immediately behind and above the aorta (Ao). The vagus nerve (V) was also undamaged. The patient made an uneventful recovery.

if the bullet was allowed to remain in place.

Ten days following admission, the patient was taken to the operating room where, through a left thoracotomy, the chest was explored and the bullet removed. As predicted, this was lodged against the trachea, on the posterior surface of the aortic arch and immediately between the left subclavian and carotid arteries (Figure 11). All of these structures appeared grossly intact. The patient made an uneventful recovery.

Comment

These cases are examples of penetrating wounds of the thorax which necessitated formal thoracotomy. Three of them were operated upon because of suspected intrathoracic complications and the fourth because of the depressed mental state of the patient.

In two of the cases, a thoraco-abdominal approach was used. In one of these (Case No. 1), the approach was through a single incision, whereas in Case No. 2, the thoracotomy was carried out through a separate incision. In Case No. 3, a myocardial laceration was suspected and operation was carried out immediately, while the nature of the injury in Case No. 4 resulted in a delayed thoracotomy.

The question of whether or not to remove retained intrathoracic foreign bodies was extensively reviewed following the second World War.[2,5] In general, small objects (one to two centimeters or less) were not removed unless they were near a vital mediastinal structure. Early removal was recommended in these cases since an operation after a complication had developed was found to carry a greater risk to the patient. The last patient presented (Case No. 4) was initially not felt to fall into this category by all the examining physicians. Operative removal was finally decided upon because of the patient's anxiety over his eventual fate if the bullet were left in place.

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Continuing Education

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April 24-26—To be held at the Nolte Center for Continuing Education, Minneapolis Campus under the direction of J. Roger Edson, M.D. Regular fee: $125; Write Director, Continuing Medical Education, Nolte Center for Continuing Education, U of M, Minneapolis 55455.

Idiopathic Systemic Fibrosis

The Simultaneous Occurrence of Retroperitoneal Fibrosis and Desmoid Tumor

ARTHUR J. MATAS, M.D.* and ARNOLD J. KREMEN, M.D.*

A case of the simultaneous occurrence of desmoid tumor and retroperitoneal fibrosis is presented. Although desmoid tumor has been described as pathologically similar to other entities included under the label systemic idiopathic fibrosis, its concomitant occurrence has not been reported previously.

RETROPERITONEAL FIBROSIS was first described in 1909 by Albarran.[1] However, it was not until 1948 that Ormond[2] described the first case in the English literature and since that time over 300 cases have been reported. More recently, retroperitoneal fibrosis has been described with similar pathological processes in other anatomical locations under the rubric "systemic idiopathic fibrosis"[3]. Mediastinal fibrosis, sclerosing cholangitis, pseudotumor of the orbit, retractile mesenteritis. and Reidel's thyroiditis have been included in this entity. All of these have been associated with retroperitoneal fibrosis in isolated cases.

Dupuytren's contracture, Peyronie's disease, and desmoid tumor have been considered possible members in this group since they are histologically similar[4]. However, they have never been reported to occur in association with any of the manifestations of systemic idiopathic fibrosis. This paper reports a case of the concomitant occurrence of desmoid tumor and retroperitoneal fibrosis, suggesting that desmoid tumor may indeed be considered as one of the manifestations of systemic idiopathic fibrosis.

Case Report

A 55-year-old female presented with a three-month history of a nontender right lower quadrant mass and some vague abdominal discomfort. There was no history of gastrointestinal or urinary tract symptoms or loss of weight. The mass had not enlarged since first noticed.

Previous surgery included hysterectomy and bilateral salpingo-oophorectomy for benign ovarian disease one year ago and appendectomy 40 years ago. There was no history of methysergide ingestion.

The patient appeared to be a remarkably healthy 55-year-old female. Physical examination was normal with the exception of scars in the lower midline and right lower quadrant of the abdomen. A large (15 x 15 cm.), nontender, nonpulsatile mass was present in the right lower quadrant extending from above the umbilicus to the pubic tubercle and from the right midaxillary line across the midline. The mass did not disappear with contraction of the anterior abdominal muscles and was not palpable on rectal examination. Peripheral pulses were present and there was no leg edema.

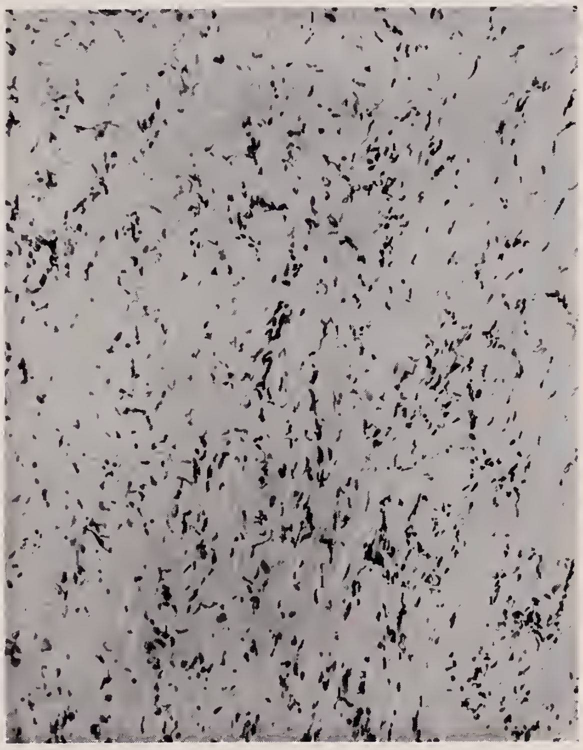

Fig. 1—Desmoid tumor showing cellular and acellular fibrous tissue with scattered chronic inflammatory cells. (x 100).

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*Department of Surgery, Mt. Sinai Hospital, Minneapolis and the Department of Surgery, University of Minnesota, Minneapolis.

Roentgenologic examination of upper gastrointestinal tract including the small intestine showed superior displacement of the third and fourth portions of the duodenum, possibly secondary to an intraabdominal mass. Intravenous pyelography was normal and barium enema examination showed a constant inferior deviation of the transverse colon. Chest Xray, electrocardiogram, hemogram, urinalysis, electrolytes, and liver enzymes were normal. (Serum total protein was 6.7 gm%, blood urea nitrogen was 19 mg%, and creatinine 0.7 mg%.)

At laparotomy, the mass was found to have two components—a large, pale, rubbery anterior abdominal wall component involving most of the thickness of the anterior abdominal wall and connected laterally to a retroperitoneal component which was mainly midline, periaortic, and below the greater curvature of the stomach, pushing the pancreas and omentum forward. The ureters and both kidneys were not involved. Biopsies were taken of both masses. No other procedures were undertaken and recovery was uneventful.

Histologic examination of sections of the anterior abdominal wall mass showed fibromatosis consistent with desmoid tumor (Figure 1), while those of the retroperitoneal mass showed fibrosis with chronic perivascular inflammation consistent with retroperitoneal fibrosis (Figure 2).

The etiology of retroperitoneal fibrosis is unknown. An association with methysergide has been shown and Suby[5] reported resolution of the process with discontinuation of the drug. The concurrence of retroperitoneal fibrosis with similar pathological process in the mediastinum,[6-9] orbit,[6] extrahepatic biliary tree,[6,10,11] thyroid[6,10,12,13] and mesentery[14] has led to the theory that these are manifestations in separate locations of the same systemic disease of areolar and adipose tissue labeled "idiopathic systemic fibrosis".[3] Comings reported two brothers, offspring of a first cousin marriage, who between them had all of the aforementioned processes.[6]

In support of a systemic theory are reports of a concomitant arthritis or arteritis. The patients tend to have increased serum globulin, mild anemia, and an increased sedimentation rate. Mulvaney[15] reported mild vasculitis in periureteral adipose tissue around the area of frank fibrosis in two patients, while Hoffman[16] described generalized arteritis (liver, muscle, kidney) in two cases, further substantiating a systemic theory.

This report suggests that desmoid tumor be added to the list of manifestations included under the entity "systemic idiopathic fibrosis".

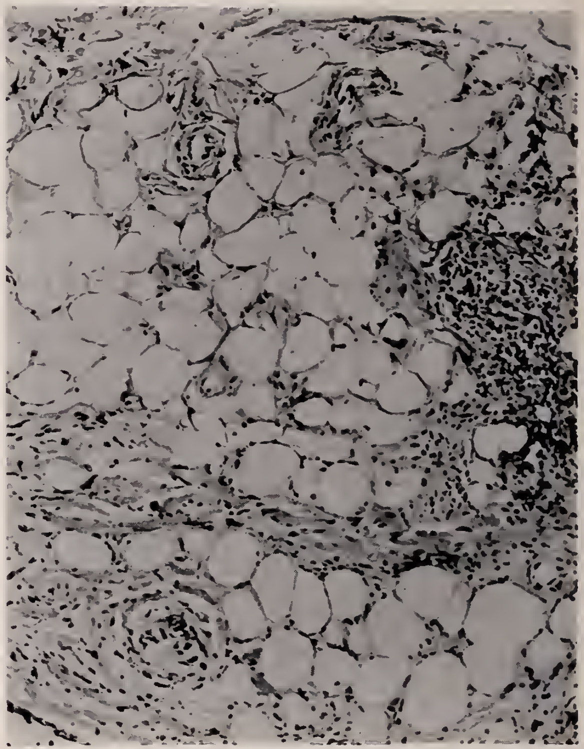

Fig. 2—Fibrous and fibroblastic infiltration of retroperitoneal adipose tissue with evidence of vasculitis (x 100).

The natural history of retroperitoneal fibrosis is unknown as there are no symptoms associated with its onset. Ormond[17] described three stages of the disease: (a) incidence and development, (b) activity and spread, and (c) contracture of the fibrotic mass. Although nonspecific abdominal pain may occur in the second stage, symptoms usually develop when, during the third stage, tubular structures, most often the ureters, become encased in the fibrotic process. The presenting symptom in 38 of 40 cases Mitchinson[18] reported was related to ureteral obstruction. Once fibrosis and contracture has occurred, the disease does not progress. Because of this, surgical relief of obstruction has been associated with a satisfactory prognosis.[19] Steroids have been tried in the active stage of the disease but information about their usefulness is inadequate at this time.[9]

References will be found on page 334.

Controlled Roentgen Examination of the Small Bowel

CHARLES M. NICE, JR., M.D., PH.D.*

A group of 210 asymptomatic young adults were given a barium meal of various kinds and a single roentgenogram of the abdomen was taken of each subject one hour later. Various factors affecting mobility and roentgenographic pattern of the small bowel were studied.

With preliminary cleansing of the colon and with the subject in the right lateral recumbent position, the use of ten ounces or more of any type of orally ingested barium suspended in plain water, followed by the oral ingestion of 10 ounces of water thirty minutes later, will produce a rapid uniform filling of small intestine resulting in an excellent diagnostic pattern.

If the colon has not been prepared, the use of a rectal suppository, the addition of a small amount of water-soluble contrast to the barium, or both, may yield comparable results.

As EARLY AS 1936, Pendergrass et al.[10] stated that it is necessary to have a standard technic for study of the small intestine. The principal requirement is to have a predictable pattern which may be judged as normal or abnormal. From a practical standpoint the transit time may be of importance to save time and film, and agents which increase or decrease the transit time may affect the pattern. A third factor is the volume of the contrast agent, which may affect both the pattern and transit time.

The type of barium suspension [1,3,6,7] has been stated to be of great importance in the production of a predictable pattern. The chief objection to the use of U.S.P. barium is that it flocculates in the presence of mucus and flocculation of the barium may then occur in normal subjects. Various substances[7] have been added to stabilize the barium suspension. On the other hand, it has been suggested that idiopathic steatorrhea[1] may be detected more readily with a flocculating medium. Sorbitol and sodium citrate[2] have been suggested as suspending agents. Miller[7] reviews the general subject of barium as a contrast agent.

The ingestion of cold saline[13] is said to decrease transit time. The small bowel enema,[10,11] after intubation of the duodenum, provides a rapid, uniform filling of the small intestine. The use of purgatives,[10] parenteral neostigmine,[5] and the addition of small doses of water-soluble contrast to the barium suspension[4] have been suggested to decrease transit time while still preserving a predictable diagnostic pattern. Reflux examination of the small bowel following barium enema[8] is said to be a rapid method for accurately demonstrating localized or stenosing lesions, especially the distal part of the small intestine.

Experiments on Normal Subjects

The opportunity arose to investigate some of the above factors when, in the Spring of 1959, the Department of Physiology requested that the first year class of Tulane Medical School be divided into small groups to observe fluoroscopy of the upper gastrointestinal tract. A total of 106 students were divided into 12 groups of five to 12 each. The only preparation required was that they ingest nothing by mouth for six hours before the study.

Although it has been stated that gastric emptying does not influence small intestinal transit time[9] it is common knowledge that the stomach empties more uniformly in the right lateral recum-

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Presented at the 39th Carman Lecture at the meeting of the Minnesota Radiological Society, September 15, 1973.

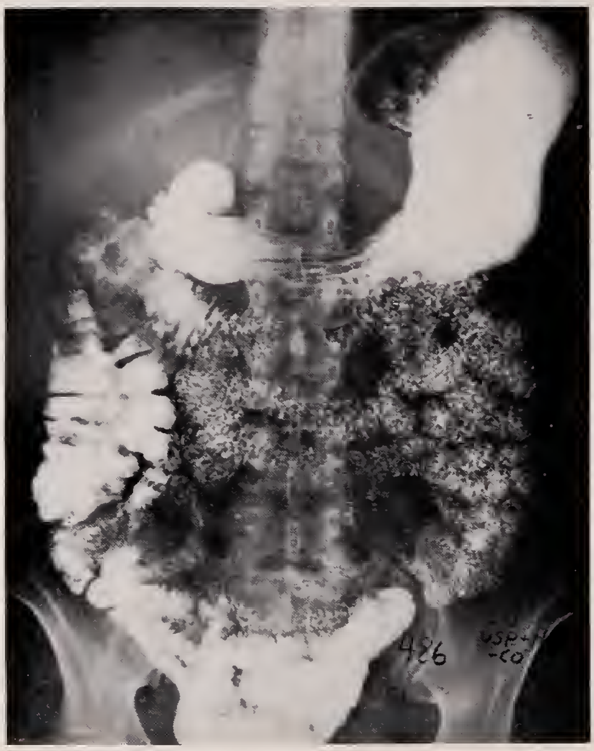


Fig. 2—Barium plus Hypaque. This patient had vague abdominal discomfort and nausea. Since no laxative had been given, one tablespoonful of powdered Hypaque (water soluble) was added to the barium suspension only the one-hour roentgenogram is shown.

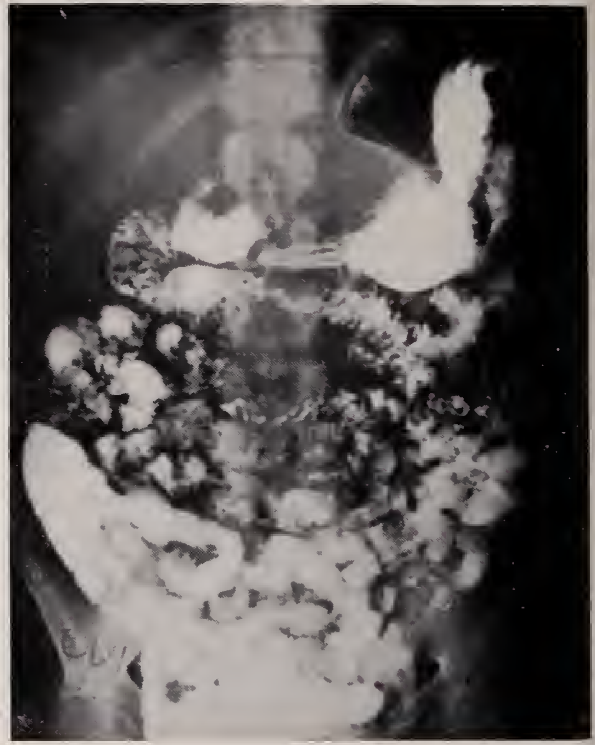


Fig. 3—Malabsorption showing minimal distortion of U.S.P. barium pattern. It is doubtful whether any abnormality would be detected with non-flocculating barium.

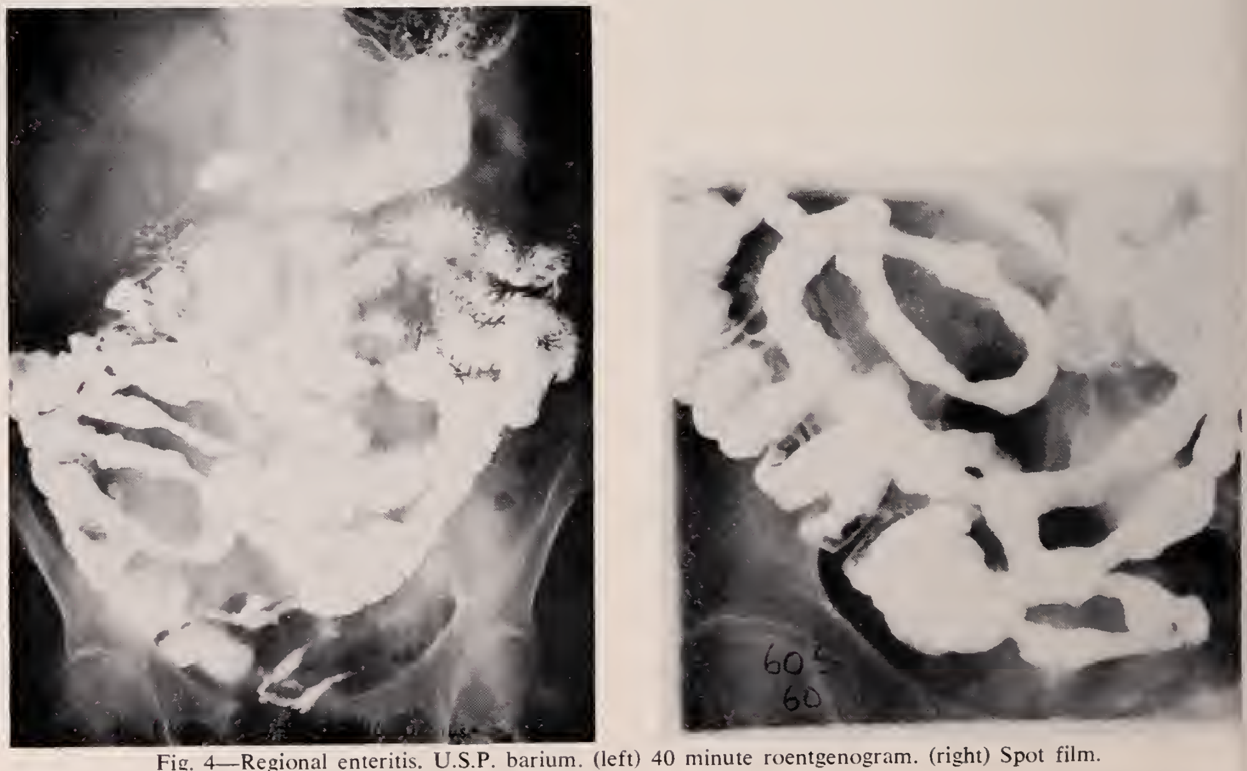
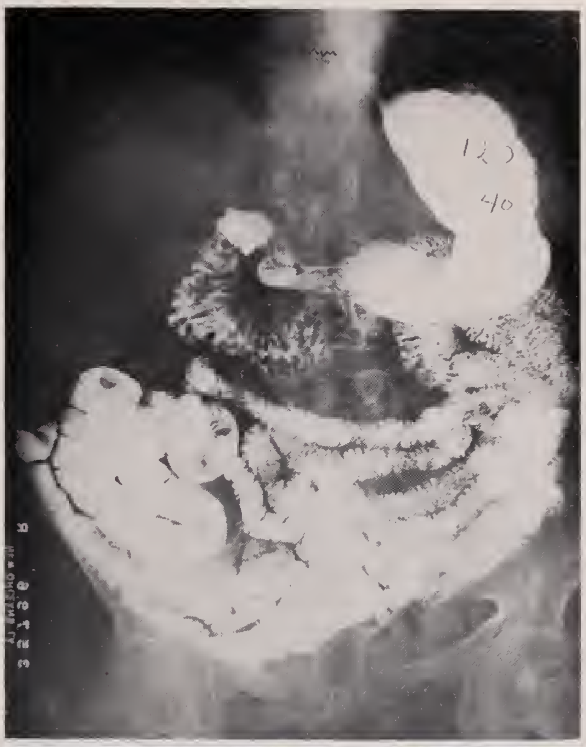


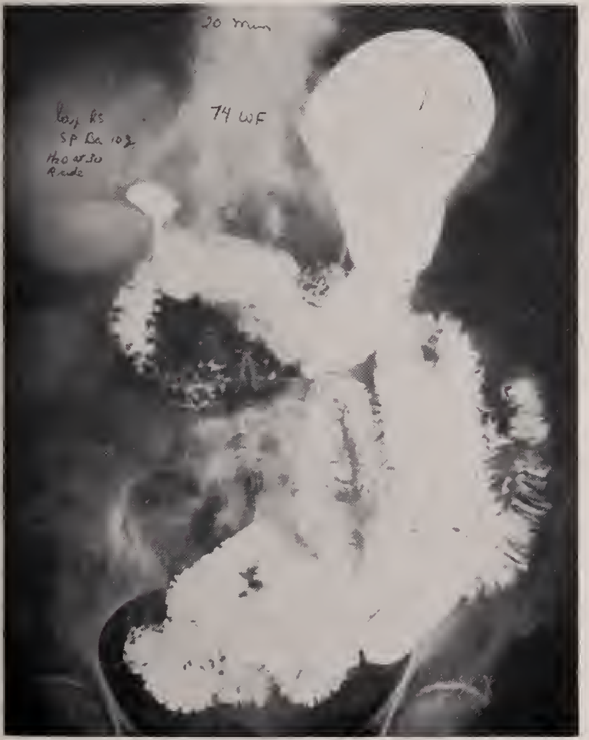
Fig. 4—Regional enteritis. U.S.P. barium. (left) 40 minute roentgenogram. (right) Spot film.

bent positions. It has also been observed that when small volumes of six ounces or less are ingested the barium tends to undergo segmentation. Therefore a minimum volume of 10 ounces was used in all of the groups. Suspension of U.S.P. barium, micronized barium, barium with saline or two percent sodium carboxymethylcellulose were tested with groups of subjects who were upright or in the right lateral recumbent position. Details of this experiment[9] have been reported.

Each subject had a single roentgenogram one hour after ingestion of the barium suspension employed. The most important factor determining whether the head of the barium column reached the colon in one hour was the presence or absence of feces in the cecum. The use of adequate volume and the assumption of the right lateral recumbent position assured a continuous pattern. In subjects remaining upright there was a tendency for micronized barium or the barium with sodium carboxymethylcellulose to produce a more desirable pattern than the plain barium or any of the forms of barium followed by the later ingestion of water or saline as tested. The taste of the saline was quite objectionable.

The second clinical experiment in the Spring of 1960 was carried out with a laxative (two ounces of castor oil) given the night before the examination. Four major plans were followed:





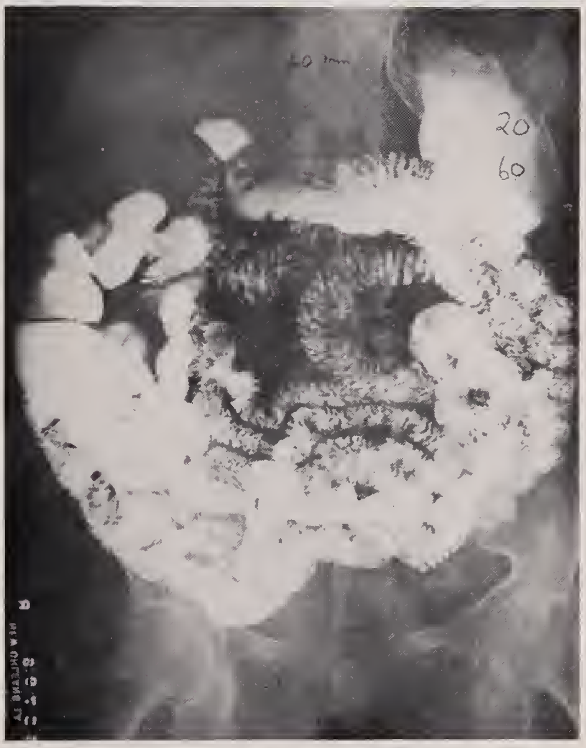


Fig. 1—Normal small bowel. This patient received a laxative the night before, ingested 10 ounces of U.S.P. barium suspension, assumed the right lateral recumbent position, and had roentgenogams (bottom-left) at 20, (top-right) 40, and (bottom-right) 60 minutes later.

Group I: Ten ounces of U.S.P. barium; subject remaining upright.

Group II: Ten ounces of U.S.P. barium; 10 ounces of water 30 minutes later; subject remaining upright.

Group III: Ten ounces of U.S.P. barium; subject in right lateral recumbent position.

Group IV: Ten ounces of U.S.P. barium; 10 ounces of water 30 minutes later; subject in right lateral recumbent position.

The results of this experiment have also been reported in detail.[9]

Discussion

The two experiments described above included a total of 210 asymptomatic young adults receiving a barium meal followed by a single roentgenogram of the abdomen one hour later. Preliminary cleansing of the colon, the use of a minimum of 10 ounces of orally ingested barium suspension, and the assumption of the right lateral recumbent position all favor a rapid uniform filling of the small intestine with the production of a desirable roentgen pattern. With this method segmentation does not occur in the normal subject with U.S.P. or other forms of barium. There is a tendency for the use of saline to produce an undesirable pattern with poor definition. If the colon has not been emptied a rectal suppository may be given or a small amount of water-soluble contrast agent (10 ml. gastrografin or one tablespoonsful of powdered hypaque) may be added to hasten transit without grossly affecting the patterns. In several thousand examinations the examinations have been completed in 60-90 minutes. More time is required in patients with an obstructing lesion or in various deficiency diseases which decrease motility of the small intestine. These conditions include tumors, regional enteritis, various forms of steatorrhea, collagen diseases, Whipple's disease, nutritional disturbances, amyloidosis, and others listed under the general terms of deficiency pattern or disordered motor function.

Examples of the use of the controlled small bowel study in normal and abnormal conditions are shown in Figures 1-4.

There may be some individuals who still insist on using the so-called nonflocculating barium. As long as the controlled method described above is used satisfactory results will be obtained. However, it is still possible that the most minimal changes are seen with U.S.P. barium because the treated barium suspensions resist change and the earliest sign of disease noted will be increase or decrease in caliber. The reflux method of Miller[8] will still prove to be useful in stenotic lesions and localized lesions low in the ileum.

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Minnesota State Medical Association

121st Annual Meeting of the Minnesota State Medical Association will be held in Duluth, May 16 and 17, in the Duluth Arena-Auditorium.

Fatal Mumps Myocarditis

JAMES C. KUSSY, M.D.*

The clinical and autopsy findings of a fatal case of mumps myocarditis are presented. The heart failure was quite rapid causing death on the third day of illness. Past studies show that electrocardiographic evidence of myocardial involvement is not uncommon but that death from myocardial involvement is very rare.

MUMPS COMMONLY INVOLVES organs such as the testes and pancreas in addition to the salivary glands. Not well known is its involvement of the heart which occurs in from four to 15% of cases.[1-3] Three cases of fatal mumps myocarditis have previously been reported in the literature.[4-6] This is the fourth such case to be reported.

Case Report

A nine-year-old boy developed bilateral parotid swelling during a mumps epidemic. He had always been healthy. He was kept at home once he showed signs of illness. On his second day of illness he ate little but was more thirsty than usual. He did not complain of headache or dyspnea. On the third day, however, he described pain in his chest and "stomach." His mother noted that he was perspiring and "felt cool." He was restless, frequently getting up and lying down. At 11:30 p.m. he went to the bathroom and then returned to the living room where his mother was sitting up with him. Shortly after lying down he was observed by his mother to sigh deeply twice and to then become noticeably quiet. She checked his pulse and obtained none and the boy was pronounced dead by the family physician.

Autopsy

Postmortem examination revealed a mild generalized edema. The heart weighed 260 grams enlarged for his age and bodyweight. Valves were normal. Coronary arteries were widely patent with no lesions. The myocardium had a normal color and consistency. No anomalies were present.

The lungs each weighed 300 gm with a moderate edema. The liver and the kidneys appeared unremarkable. The spleen was moderately congested weighing 200 gm. The brain appeared normal.

On microscopic examination the heart throughout the ventricles showed inflammatory cells occasionally separating muscle fibers. These were mononuclear cells, plasma cells and polymorphonuclear leukocytes. Rarely an individual muscle fiber was necrotic within or next to an area

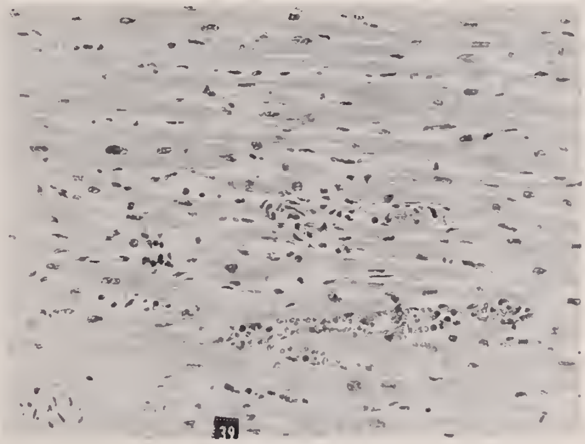

Figure 1

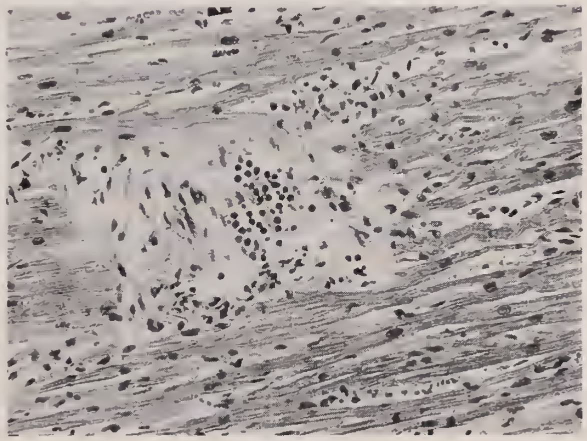

Figure 2

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*St. Gabriel's Hospital, Little Falls, Minnesota.

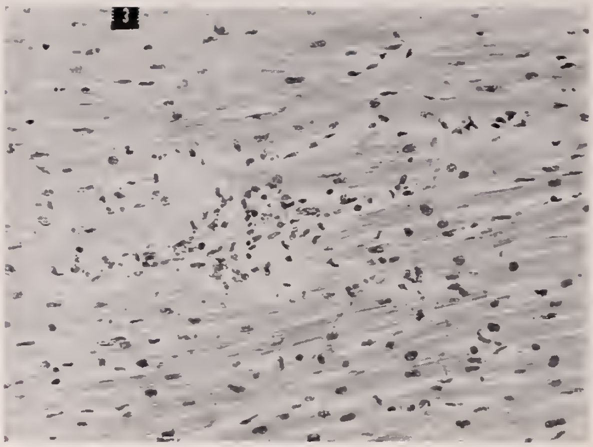

Figure 3

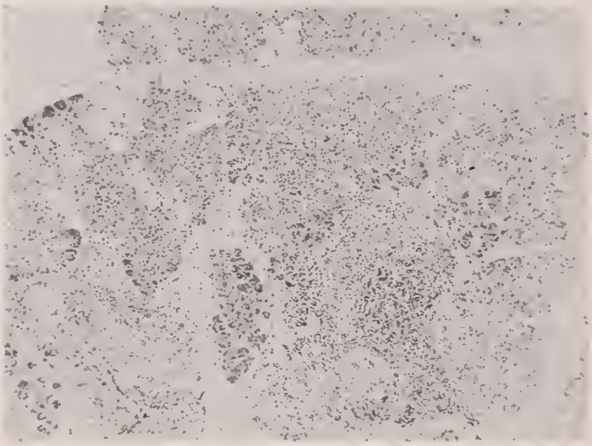

Figure 4

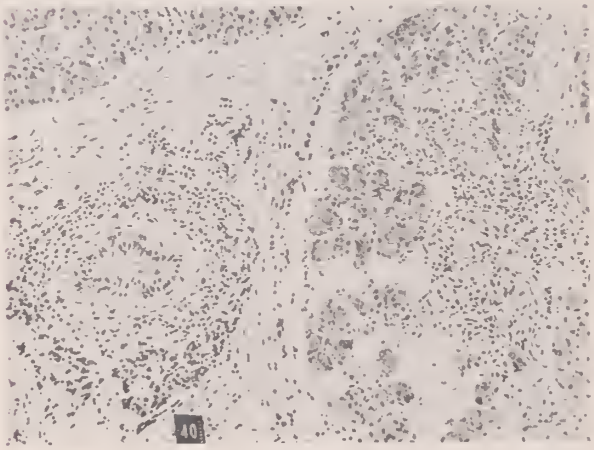

Figure 5

of inflammatory exudate.

The parotid gland microscopically showed a marked inflammation with many round cells and some polymorphonuclear leukocytes. The acinar cells uniformly had cytoplasmic inclusion bodies (Figures 4 and 5).

The pancreas, testes, and brain appeared unremarkable.

Discussion

Fatal mumps myocarditis is a very rare occurrence. This is the fourth such case reported in the literature. It differs clinically from the other cases in that the death occurred on the third day of illness whereas the others occurred 14 days, 55 days, and eight months after the onset of illness. A near fatality has been recently reported from Africa.[7]

Although a fatal result then is rare, involvement of the heart by the mumps virus is not uncommon. Various studies in which mumps patients have been studied with electrocardiograms have shown abnormalities appearing during their illness and disappearing upon recovery in 15.4%, 5%, 6.7% and 4.4% of the cases.[1-3,8] The most frequent electrocardiographic changes found are depression of the S-T segments and flattening or inversion of the T wave. The majority of these cases showed no clinical evidence of myocardial involvement.

Acknowledgment

The review of this manuscript and the photography provided by Dr. Jesse E. Edwards is greatly appreciated.

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*Shakespeare: Hamlet, V.ii. 358-359. c. 1600.

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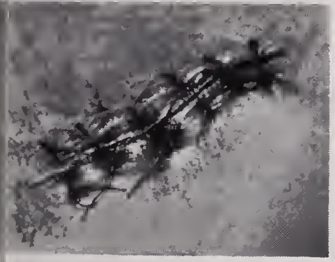

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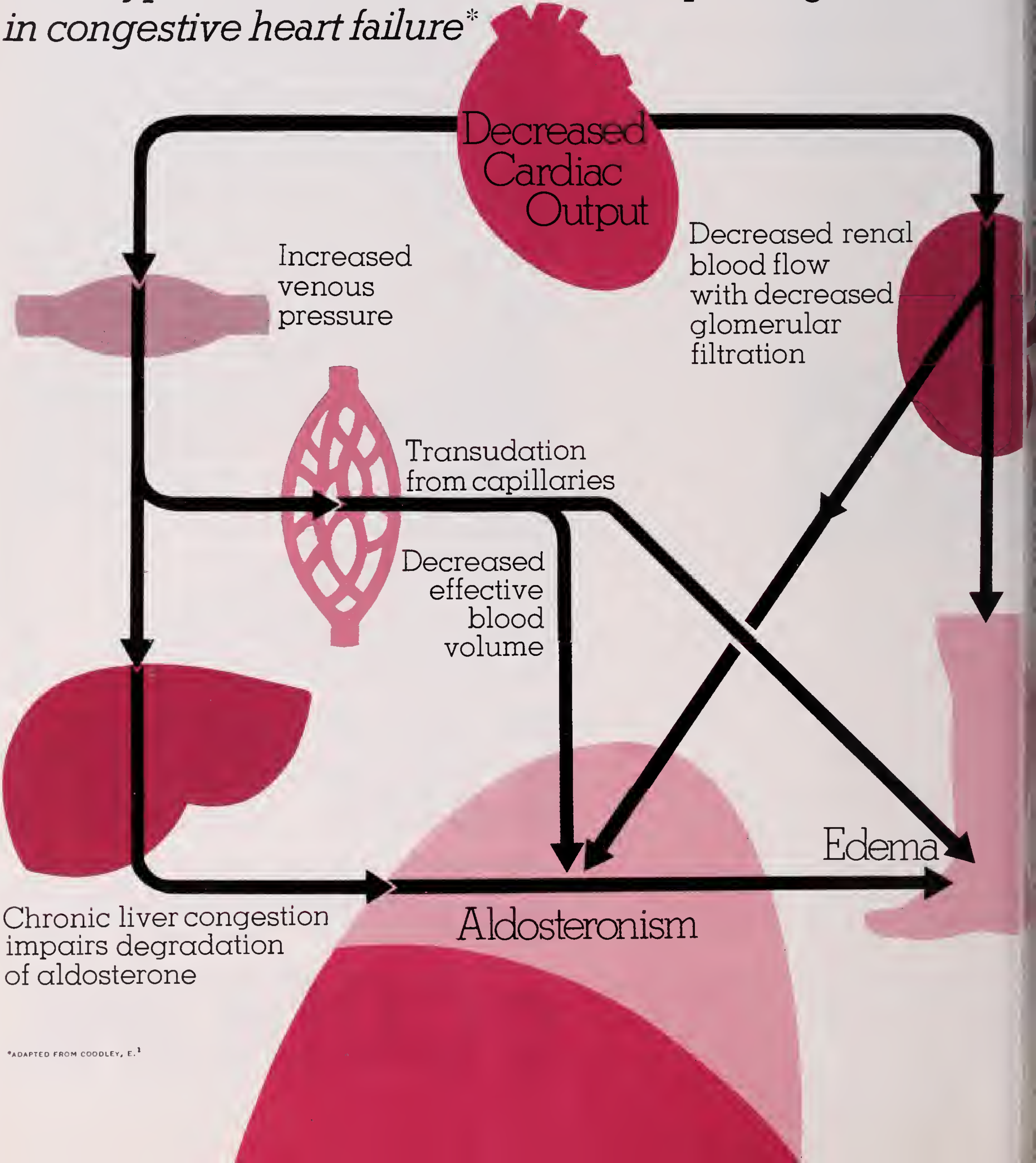
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Aldactone plus "A.D.D." schedule
inimizes potassium deficiency and
otentiates effect of "add-on" diuretic.[2]
Avoids acute volume depletion and
ldosterone rebound.[2]

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daily dose of a thiazide
Permits daily additive diuretic effect
hile maintaining potassium balance.

Indications—Essential hypertension; edema or ascites of congestive heart failure, cirrhosis of the liver and the nephrotic syndrome; idiopathic edema. Some patients with malignant effusions may benefit from Aldactone (spironolactone), particularly when given with a thiazide diuretic.

Contraindications—Acute renal insufficiency, rapidly progressing impairment of renal function, anuria and hyperkalemia.

Warnings—Potassium supplementation may cause hyperkalemia and is not indicated unless a glucocorticoid is also given. Discontinue potassium supplementation if hyperkalemia develops. **Usage of any drug in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the mother and fetus.**

Precautions—Patients should be checked carefully since electrolyte imbalance may occur. Although usually insignificant, hyperkalemia may be serious when renal impairment exists; deaths have occurred. Hyponatremia, manifested by dryness of the mouth, thirst, lethargy and drowsiness, together with a low serum sodium may be caused or aggravated, especially when Aldactone is combined with other diuretics. Elevation of BUN may occur, especially when pretreatment hyperazotemia exists. Mild acidosis may occur. Reduce the dosage of other antihypertensive drugs, particularly the ganglionic blocking agents, by at least 50 percent when adding Aldactone since it may potentiate their action.

Adverse Reactions—Drowsiness, lethargy, headache, diarrhea and other gastrointestinal symptoms, maculopapular or erythematous cutaneous eruptions, urticaria, mental confusion, drug fever, ataxia, gynecomastia, inability to achieve or maintain erection, mild androgenic effects, including hirsutism, irregular menses and deepening voice. Adverse reactions are infrequent and usually reversible.

Dosage and Administration—For **essential hypertension** in **adults** the daily dosage is 50 to 100 mg. in divided doses. Aldactone may be combined with a thiazide diuretic if necessary. Continue treatment for two weeks or longer since an adequate response may not occur sooner. Adjust subsequent dosage according to response of patient.

For edema, ascites or **effusions** in **adults** initial daily dosage is 100 mg. in divided doses. Continue medication for at least five days to determine diuretic response; add a thiazide or organic mercurial if adequate diuretic response has not occurred. Aldactone dosage should not be changed when other therapy is added. A daily dosage of Aldactone considerably greater than 75 mg. may be given if necessary.

A glucocorticoid, such as 15 to 20 mg. of prednisone daily, may be desirable for patients with extremely resistant edema which does not respond adequately to Aldactone and a conventional diuretic. Observe the usual precautions applicable to glucocorticoid therapy; supplemental potassium will usually be necessary. Such patients frequently have an associated hyponatremia—restriction of fluid intake to 1 liter per day or administration of mannitol or urea may be necessary (these measures are contraindicated in patients with uremia or severely impaired renal function). Mannitol is contraindicated in patients with congestive heart failure, and urea is contraindicated with a history or signs of hepatic coma unless the patient is receiving antibiotics orally to "sterilize" the gastrointestinal tract.

Glucocorticoids should probably be given first to patients with nephrosis since Aldactone, although useful for diuresis, will not directly affect the basic pathologic process.

For **children** the daily dosage should provide 1.5 mg. of Aldactone per pound of body weight.

References: 1. Coodley, E.: Consultant 12:106-107, 109, 111, 113, 115 (July) 1972. **2.** Thorn, G. W., and Louler, D. P.: Am. J. Med. 53:673-684 (Nov.) 1972.

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Editorials

Mastoid Ecchymosis

CAREFUL CLINICAL evaluation of the patient continues to be vital in medical practice. By their reminder of the occurrence of mastoid ecchymosis (Battle's sign) in the basal skull fractures, and of the importance of careful examination of such patients, Alter et al.* emphasize this important fact.

The irregularity of the bones of the base of the skull and the difficulty in radiologic visualization of this area, particularly in obtunded or sick patients, prevent the identification of many basal skull fractures by x-ray examination. Yet a fracture in this region is particularly serious because of the close relationship of the cranial nerves, pituitary, hypothalamus, major intracranial vessels, and brainstem, to these bones. In addition, such fractures can involve paranasal sinuses, or produce cerebrospinal fluid rhinorrhea or otorrhea with a significant risk of subsequent intracranial infection.

Ecchymosis in the mastoid region appearing within hours or days after head injury provides strong clinical evidence for the presence of a basal skull fracture, particularly when bleeding from the ear on the same side, or a cranial nerve lesion such as a sixth nerve palsy, are also found. Even if radiologic study of the skull bones does not allow visualization of the fracture line, the presence of such signs should be enough to prompt the diagnosis and appropriate management.

Allan J. D. Dale, M.D.
Consultant, Department of Neurology
Mayo Clinic

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*See page 263.

Primary Thrombosis of the Subclavian Vein

OLIN IN THE FEBRUARY ISSUE* has presented a concise summary of the diagnosis, treatment and pathogenesis of primary thrombosis of the subclavian vein. This is a rare condition but interesting as it points out the difficulty in determining clearly the etiology of venous thrombosis. In his case report there seems to be no apparent etiology. In the majority of reported cases mild trauma is the only initiating factor noted. Other causes or predisposing factors to venous thrombosis such as malignancy, fracture, hematomas, heart disease (cardiac decompensation), both control pills and coagulation abnormalities should be noted or ruled out.

The fact not a single case of embolization has been reported with primary thrombosis of the subclavian vein is interesting. The etiology, treatment and pathogenesis seem to be the same as primary thrombosis in other veins.

Gene R. Hartman, M.D.
Minneapolis, Minnesota

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*Olin Ronald: Primary thrombosis of the subclavian vein. Minnesota Med 57:93, 1974.

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Isoniazid Toxicity

The interesting report on isoniazid (INH) toxicity by Patrick E. Mottram et al.* in the February issue of Minnesota Medicine teaches us some important lessons. It is increasingly evident that members of certain of the subcultures of our society will, quite literally, take anything in order to get a "kick" or a "high". The physician, with his professional respect for drugs, cannot really understand the insouciance with which a person will receive a completely unknown foreign material into his body by ingestion, inhalation, or injection.

A companion lesson, of course, is the importance of an accurate history in the evaluation of a patient's situation. When the patient is unconscious or unable to communicate for some other reason, other sources of historical data must be explored to the fullest extent, including gaining information from family, from friends, and perhaps even from an inspection of the premises in which the patient has been living, in order that no clue to an accurate diagnosis may be overlooked.

We are reminded once again of the importance of understanding fundamental mechanisms of the production of disease and of the action of drugs. Both the accurate knowledge about the drug involved and a thorough understanding of the mechanism of its action were necessary in the successful treatment of the patient, whose case is reported by the authors. INH is known to form a complex with pyridoxine (Vitamin B_6) or, probably more precisely, with one of the derivatives of pyridoxine, resulting in incomplete activation of this vitamin. Pyridoxine serves many functions within the body, as a coenzyme for vital metabolic processes affecting at least the skin, the muscles, the hematologic system, and the central nervous system. Pyridoxine was a logical and apparently effective antidote in this unusual case of poisoning, but its use required special insights on the part of the responsible physicians.

Robert B. Howard, M.D.
Abbott-Northwestern Hospital

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*Mottram PE et al: Isoniazid toxicity. Minnesota Med 57:81, 1974.

Extractions in Hemophilia

As Short and Ogle* point out in the February issue of Minnesota Medicine, post-operative administration of the synthetic anti-fibrinolysin epsilon aminocaproic acid (EACA) in combination with adequate preoperative factor VIII replacement has proven effective in preventing hemorrhage following dental extractions in patients having hemophilia. With an adequate level of factor VIII at the time of surgery, the hemophiliac is able to form a firm clot in the surgical wound. EACA exerts its effect by inhibiting normal clot lysis during wound healing. This is important since it conserves supplies of factor VIII concentrate, reduces complications such as hepatitis and factor VIII antibody production, and shortens hospital stay.

The effectiveness of this therapy in other surgical procedures in hemophiliacs has yet to be demonstrated. Patients with hemophilia do not have increased fibrinolysis and the prophylactic administration of EACA to prevent spontaneous hemorrhage is not effective and in fact may be dangerous. The use of EACA has also been used to control hematuria in hemophilia but is no longer recommended since it may result in ureteral obstruction by blood clot which is resistant to lysis by urokinase.

C. R. Chedister, M.D.
Minneapolis, Minnesota

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*Short SG and Ogle RG: Extractions in hemophilia. Use of EACA. Minnesota Med 57:77, 1974.

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Pseudotumor Cerebri

Benign increased intracranial pressure or pseudotumor cerebri presents a challenging diagnostic problem for all clinicians. The Shapiros* have pointed out the known etiologic factors, diagnostic criteria, clinical course, and treatment in this condition.

Although pseudotumor cerebri by definition is a benign condition, the etiological factors presented by the authors are not entirely benign. Patients with this condition respond to proper treatment. Ventriculography and pneumoencephalography in some circumstances can be delayed if the criteria for the diagnosis of pseudotumor cerebri are fairly clear-cut: headaches, papilledema, elevated spinal fluid pressure in an otherwise normal spinal fluid examination, and completely normal neurological examination. However bilateral angiograms should be carried out in all cases to exclude subtle intracranial lesions. The angiogram may also outline whether or not there is enlargement of the ventricular system. This, together with a normal EEG and brain scan in an otherwise healthy individual, can usually warrant initial treatment before considering the more difficult diagnostic studies mentioned above.

Osmoglyn is a 50 percent glycerin solution used in children and adults for reduction of increased intracranial pressure. It is also used to reduce intraocular pressure in patients developing glaucoma. I do not use this substance in the treatment of pseudotumor cerebri, but as the authors point out, the treatment should be individualized for each patient. The use of Decadron continues to be the most successful treatment for this condition. I use doses up to 16 mg. for the first five to seven days of treatment and then gradually taper off to an oral dosage much as the authors have stated in their article. This has proved to be successful in returning these patients to a normal state. The cerebral spinal fluid pressure may return to normal before the papilledema subsides.

I concur with the authors' suggestion that the progress of treatment in these patients should be done in conjunction with a neuro-ophthalmologist, and funduscopic pictures can be of considerable value in documenting the patients' improvement.

Richard F. Galbraith, M.D.
Minneapolis Clinic of Psychiatry and Neurology

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*Shapiro SK and Shapiro Irving: Pseudotumor Cerebri. Minnesota Med 56:1021, 1973.

Mesonephric Carcinoma of Cervix

Since the original article by Herbst, et al.,[1] describing the association of adenocarcinoma of the vagina in girls and young women with maternal estrogen ingestion (diethylstilbesterol), a great deal of attention has been focused on this entity. Fortunately, the incidence of this and associated tumors in female offsprings of women treated with this drug in pregnancy is low. Nevertheless, any female child so exposed during intrauterine life should be followed closely with pelvic examinations, Pap smears, and biopsies when indicated.

The paper by Noller, et. al.,* in the February issue of Minnesota Medicine is unique in that this young woman was pregnant at the time the diagnosis was made. Credit must be given to the primary physician whose index of suspicion was high enough to prompt him to biopsy the area leading to a definitive diagnosis and thence to treatment which may result in a cure. One cannot over emphasize the importance of a careful pelvic examination in girls and young women with abnormal discharge and (or) bleeding.

Thomas C. Carrier, M.D.
Minneapolis, Minnesota

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*Noller, K. L. et al:. Mesonephric Carcinoma of Cervix. A Case Associated with Intra-Uterine Pregnancy. Minnesota Med 57:97, 1974.

Reference

1. Herbst AL; Ulfelder H, Poskanzer, DC: Adenocarcinoma of the vagina: association of maternal stilbestrol therapy with tumor appearance in young women. N Engl J Med 284:878, 1971.

Late Toxic Effects of Cytotoxic Drugs

THE PROBLEM OF late toxicity consequent to the prolonged use of cytotoxic chemotherapy has become a real concern. Whereas the treatment of advanced cancer previously was almost universally ineffective, the advent of more effective chemotherapy and treatment schedules has provided significant and prolonged control for some patients. The earlier use of cytotoxic chemotherapeutic agents, employed as adjuncts to primary surgical and/or radiotherapeutic approaches, has dramatically altered the course of some cancers. The success of combination chemotherapy, and particularly the success of some adjuvant chemotherapy programs, will undoubtedly promote further investigational trials in a variety of tumor systems and patient populations.

Fortuny and Theologides' article* on the Late Toxic Effects Following the Prolonged Administration of Cytotoxic Drugs has very well documented the occurrence and spectrum of toxicity associated with most of the commercially available agents. As pointed out, irreversible and severe organ system disease can be a possible complication of effective treatment for palliation of malignant and benign disease. With earlier and more aggressive therapy of malignant disease, undesirable long-term complications of chronic chemotherapy will undoubtedly occur more frequently. The pattern of the chronic toxicity of most of these agents can be suspected from the data cited. Additive and differing toxicity associated with varying combinations of effective chemotherapy or new investigational agents yet remains to be determined. Long-term as well as acute toxicity evaluation data will of necessity be programmed into future chemotherapy trials.

Richard G. Hahn, M.D.
Department of Oncology
Mayo Clinic
Rochester, Minnesota

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*January, 1974, page 19.

President's Letter—(Continued from page 253).

recognize the difference between the authority of the hospitals' trustees over the facilities and employees of the hospital as against the physician's power to practice medicine. Not only do they fail to recognize the difference between power and authority, but often they are even confused about the limits of their own authority. These are the ones who would take over the system, who would get the hospital into the practice of medicine, and who would erect a corporate delivery system.

Physicians, loath to exercise their real strength, must recognize the difference between power and authority, must use their energy to negotiate a reasonable agreement with the hospital trustees, must do this from strength and not from weakness. For a single physician to negotiate with a multi-million dollar corporation for a staff membership, for privileges, or for any other of the many elements of medical activity within the hospital, is a grossly uneven exchange. Obviously, he must lead from strength, possibly even from corporate strength. Perhaps the physicians of the staff should band together in a corporate association. Negotiations regarding hospital-medical staff relationships then can take place between the two corporations, that of the hospital and that of the medical staff—to set up a true partnership, the function of which will be to develop an environment where excellent medical care can be rendered by physicians in a climate of understanding and respect. Resulting from this negotiation and responsible to this partnership would be the hospital administration, charged with the duty of doing the job and given the authority to get it done. Perhaps the corporate structure of physicians should even be at a level above the medical staff, possibly at the level of the local county or state medical society. From this kind of negotiation through strength can come the solution of many problems now nagging at the system and making it necessary to introduce new staff officers to their jobs by route of a Rocky Mountain honeymoon.

John J Regan

President
Minnesota State Medical Association

Letter to the Editor

Dear Editor:

An important and pertinent article was published by Short and Ogle* in the February issue, entitled, "Extractions in Hemophilia." It is important to note that problems are encountered with such therapy and that it should not be undertaken lightly.

The Hemophilia Clinic at Fairview Hospital in Minneapolis is concerned with over 125 hemophilia patients. Our experience both in prophylactic and restorative dentistry is large. Caution must be suggested against excessive optimism and inadequate precautions with such patients. EACA is contraindicated in patients with red cells in the urine or with unusual renal system history. In such situations abnormal clotting in the genitourinary system or even renal shutdown can occur because of excess antifibrinolytic activity and diminution of urokinase activity in the urine.[1,2,3]

Dental therapy is preceded by replacement therapy to raise the deficient factor to about 50-60%. EACA is then administered for 10-14 days thereafter to promote a stable contracted clot. In almost three years of such therapy only one patient has shown need for further replacement therapy. The patients are usually managed as outpatients. This method has been successful elsewhere in clinics in the United States and England.[4,5]

Lawrence J. Singher, M.D.
Director—Minnesota Hemophilia Clinic Foundation
Fairview Hospitals, Minneapolis, Minnesota

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*Short SG and Ogle RG: Extractions in hemophilia. Minnesota Med 57:77, 1974.

References

1. Singher LJ: Handbook of Hemophilia. Excerpta Medica. To be published 1974.
2. Coggins JT and Allen T: J Urol 107:647, 1972.
3. Stark S. et al.: Scand J Haemat 2:99, 1965.
4. Corrigan J: J Peds 80:124, 1972.
5. Walsh PN et al.: Brit J Haem 20:463, 1971.

Dear Editor:

In his February letter* on the A.M.A. meeting, President John J. Regan displays genuine ability in writing interesting material. I was intrigued and fascinated by his fantastic capacity for picturesque language. I faltered over "peripatetic, hucksterism and even gemutlichkeit." The real beauties John pulled out of his magic bag were "abrazzos" and "obfuscates". Obfuscate—I learned meant "to darken or to confuse"; Abrazzos—derivation Spanish meaning "to embrace as in salutation" employed in Latin America. Keep up educating us, President John, even though some of us sluggards have to sit with the dictionary at our side when we peruse your monthly letter.

Bror F. Pearson, M.D.
Shakopee, Minnesota

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*See page 75.

Erratum

"Why Have an Annual Meeting?"

Please refer to page 247 of the March issue, left column, fifth paragraph, last sentence. The sentence should read:

> "The two day session promises to be of high academic and scientific appeal, accredited by the AMA, *acceptable for 13.5 prescribed hours by the AAFP,* approved for 13.5 hours in Category 1 of the Physicians Recognition Award."

Minnesota State Medical Association Nominees for State Offices

In cooperation with the House of Delegates, we are publishing short biographies of the nominees for Minnesota State Medical Association offices. In addition, any delegate may make nominations from the House of Delegates floor after the report of the Nominating Committee.

Each elected official will assume his position at the conclusion of the 1974 Annual Meeting. The current president-elect, Doctor Barnard Hall, was elected in 1973 and will become president after the 1974 Annual Meeting concludes.

President-Elect

G. R. Diessner, M.D.

Currently the chairman of the Council, Doctor G. R. Diessner, Rochester, is a long-time leader of the Minnesota State Medical Association. He was a delegate for eight years and has been a member of many Association committees. Presently he is on the Committee on Committees, Medical School Relations Committee and Executive Committee. He represents the first district as councilor.

Outside the Association, Doctor Diessner is a member of the Southern Minnesota Medical Association which he served as secretary and president. He was also president of the Zumbro Valley Medical Society in 1965. In addition he is a member of the American Rheumatism Association, American Medical Association, Mayo Foundation Chapter of Sigma XI, Alpha Omega Alpha and is a fellow in the American College of Physicians. In 1956 he became a diplomate of the American Board of Internal Medicine.

Doctor Diessner was born in Waconia, and attended the University of Minnesota Medical School, graduating in 1942 with an M.D. degree. He received an M.S. in Medicine in 1949. In 1948 he married and he and his wife, Margaret, have four children.

He interned at Receiving Hospital, Detroit and served in the U.S. Army Medical Corps during the Second World War. After the war, he accepted a Fellow in Internal Medicine at the Mayo Foundation. Currently he is Head of the Section Rheumatology at the Mayo Clinic and Assistant Professor in Medicine, Mayo Graduate School, University of Minnesota and Assistant Professor of Medicine, Mayo Medical School.

Severin H. Koop, Jr., M.D.

St. Cloud otolaryngologist, Doctor Severin H. Koop, is currently president-elect of the Minnesota Academy of Ophthalmology and Otolaryngology and clinical assistant professor at the University of Minnesota Department of Otolaryngology. He completed his residency in 1966 and was board certified the same year.

Doctor Koop attended St. Thomas College for three years before entering the University of Minnesota Medical School where he received his M.D. degree in 1955. He interned at Ancker Hospital, St. Paul, and was in the U.S. Army medical corps for two years before entering general practice in St. Cloud, 1959-62.

He lists membership in the Stearns-Benton County Medical Society, American Medical Association and American Academy of Ophthalmology and Otolaryngology. In addition, he is on the Council of Otolaryngology of the American Academy of Ophthalmology and Otolaryngology.

Doctor Koop likes tennis, fishing, photography and skiing. He and his wife, Ruth, have six children.

First Vice-President

John J. Eustermann, M.D.

Doctor John J. Eustermann, Mankato internist, was born in Lewiston. He received his undergraduate education at St. Mary's College, Winona, and his M.D. degree from Clayton University Medical School, Omaha, Nebraska, in 1943. He interned at St. Louis University, St. Louis, Missouri, in 1943 and for two years was a flight surgeon in the U.S. Air Force. Upon leaving the service in 1946, he spent a year in the University of Minnesota Department of Internal Medicine before entering general practice at the Mankato Clinic.

In 1950 he completed his residency in internal medicine at Washington University, St. Louis, Missouri. Since that time, he has been with the Mankato Clinic Department of Internal Medicine.

Doctor Eustermann is currently the president of Mankato Clinic Ltd. He is a past president of Immanual-St. Joseph's Hospital Staff, Southern Minnesota Medical Association, Minnesota Association of Internists and Blue Earth County Medical Society. He is the immediate past president of the Minnesota Heart Association.

With the Minnesota State Medical Association, he has served on the Public Policy Committee and is presently on the Heart Committee.

Doctor Eustermann and his wife, Mary, have one daughter, Elizabeth, 17. Doctor Eustermann enjoys duck and pheasant hunting, fishing, golf and skiing.

Malcolm Fifield, M.D.

With the opening of the medical school in Duluth, Doctor Malcolm Fifield became clinical associate professor of urology and added a new dimension to his urological practice.

Doctor Fifield is board certified in urology and practices in Duluth with two associates. He is on the staffs of St. Luke's Hospital where he was chief of staff in 1973, St. Mary's Hospital and Miller-Dwan Hospital.

In 1950 he was graduated from the University of Minnesota Medical School. He interned at the U.S. Naval Hospital, Bremerton, Washington, and took his residency at the V.A. Hospital Minneapolis and the University of Minnesota.

He was president of the St. Louis County Medical Society in 1970 and has been its delegate to the Minnesota State Medical Association for the past four years. He is also a member of the Interurban Academy of Medicine and the Duluth Surgical Society which he served as president in 1968.

Doctor Fifield lists membership in the Minnesota State Medical Association, American Medical Association, Minnesota Surgical Society, and the American Urological Association. He is on the executive council of the Minnesota Chapter American College of Surgeons and for three years he was on the executive committee of the North Central Section of the American Urological Association.

Sailing and tennis fill up Doctor Fifield's free hours. He and his wife, Nancy, have four sons and three daughters.

James C. Mankey, M.D.

Minneapolis native Doctor James C. Mankey still serves the Mill City as internist.

He attended the University of Minnesota Medical School, graduating with his M.D. degree in 1943. He interned at Milwaukee County General Hospital and began his residency which was interrupted by military service. In 1948 he completed his residency at Milwaukee County General Hospital.

Doctor Mankey is a member of the Hennepin County Medical Society, American Medical Association, Minnesota Society of Internal Medicine, and Minneapolis Society of Internal Medicine.

He is board certified in internal medicine and is a fellow in the American College of Physicians.

Second Vice-President

William Jacott, M.D.

A native of Duluth, Doctor William Jacott returned there in 1964 to intern at St. Luke's Hospital and remained at the Lakeside Medical Center.

Doctor Jacott received his undergraduate degree from the University of Minnesota, Duluth, and his medical degree at the University of Minnesota in 1964. He is now clinical assistant professor at UMD Medical School.

With the Minnesota State Medical Association, Doctor Jacott has served as delegate since 1970. He is the local arrangements chairman for this annual meeting. In 1970-71 he was a member of the Nominating Committee and currently is on the Family Practice Committee.

Doctor Jacott is a member of the St. Louis County Medical Society, American Academy of Family Physicians, the Minnesota Academy of Family Physicians, and the Duluth Academy of Family Physicians which he served as president in 1973.

In addition to the medical societies, Doctor Jacott is a member of the Minnesota OB-Gyn Society, Northern Minnesota Council for Medical Education, U.M.D. Medical School Deans Advisory Committee chairman and Family Practice Curriculum Content Committee chairman, Duluth Graduate Medical Education Committee and Alpha Kappa Kappa.

He is on the staff of St. Luke's Hospital and was chief of staff at Miller-Dwan Hospital in 1971-72.

Doctor Jacott and his wife, Judith, have three children. Doctor Jacott is active in Duluth community affairs. He is a member of the Duluth Rotary Club, Lakeside Presbyterian Church, Duluth Blueline Club, U.M.D. Alumni Association, Minnesota Army National Guard Citizen's Committee and the Alworth Memorial Scholarship Board.

Within his medical profession, Doctor Jacott serves Duluth as president of Lakeview Professional Associates, and as member of the Miller-Dwan Medical Center Foundation, Duluth Hospital Council and Duluth Medical Board of Review.

Secretary

Stanley J. Antolak, M.D.

St. Paul urologist, Doctor Stanley J. Antolak, completed his urology training at the Minneapolis V.A. Hospital in 1968. Presently, he is in practice with three associates.

Doctor Antolak's medical training began at the University of Minnesota. He interned at Philadelphia General Hospital and took general surgical training at Kingsbridge V.A. Hospital, Bronx, New York, and Minneapolis V.A. Hospital. He spent six months in family practice.

He is a member of the American Urological Association and the American

Fertility Society. He is on the following St. Paul hospital staffs: Children's Hospital; Bethesda Lutheran Hospital; United Hospitals, Miller Division and St. Luke's Division. He is a clinical instructor in urology at the University of Minnesota Hospitals, Gillette Children's Hospital and St. Paul-Ramsey Hospital.

Robert L. Powers, M.D.

Rochester born Doctor Robert L. Powers received his M.D. degree in 1959 from the University of Minnesota. Following graduation, he interned at St. Joseph's Hospital, St. Paul, and since has been in family practice at the Lexington-Larpenteur Medical Center, P.A., St. Paul. Now living in St. Paul, Doctor Powers has eight children.

Doctor Powers is a Ramsey County Medical Society delegate to the Minnesota State Medical Association and current secretary of the Association. He is a member of the American Medical Association, the Minnesota Academy of Family Practice, the Civil Aviation Medical Association and is a fellow in the American Academy of Family Physicians.

Currently he is on staff at St. Joseph's Hospital, Children's Hospital and United Hospitals, St. Luke's Division, where he is also on the teaching staff. Doctor Powers is an Assistant Clinical Professor of Family Practice and Community Health at the University of Minnesota.

Treasurer

Glenn L. Petersen, M.D.

Doctor Glenn L. Petersen, now a Minneapolis anesthesiologist, was in family practice in Minneapolis for nearly 15 years before returning to the University of Minnesota as a resident, 1959-61.

Doctor Petersen received his M.D. degree from the University of Minnesota in 1944. He interned at Baltimore County Hospital.

He is past chief of staff at Fairview and Fairview Southdale Hospitals. He is past president of the Hennepin Academy of General Practice and Minnesota Society of Anesthesiology. He is a delegate from Minnesota to the American Society of Anesthesiology.

With the Minnesota State Medical Association, Doctor Petersen served on the Medical Service Committee for the past 18 years, on the Relative Value Index Subcommittee of the Committee on Medical Service for the past two years and on the Committee on Anesthesiology for the past three years. Also, he has served as the Hennepin County Medical Society delegate to the Association House of Delegates.

Doctor Petersen, better known to his friends and wife, Betty Lou, as "Skip," likes sports of all kinds—skiing, golf and tennis, particularly. He is the father of four children.

Matt K. Plasha, M.D.

Doctor Matt K. Plasha founded the Coon Rapids Clinic in 1953 and remains there in family practice. Born in Duluth in 1920, Doctor Plasha graduated from the University of Minnesota Medical School in 1945. He interned at Harper Hospital, Detroit, and served in the U.S. Army for two years. Before moving to Coon Rapids, he was in family practice in Glenwood for five years.

Doctor Plasha is a past president of the Minnesota Academy of Family Practice and an alternate delegate to the American Academy of Family Practice. For many years he has been a delegate to the Minnesota State Medical Association. He is a diplomat, American Board of Family Practice and in 1967 he served as chief of staff at Mercy Hospital, Coon Rapids.

He and his wife, Dorothy, have seven children.

Speaker of the House of Delegates

Richard E. Anonsen, M.D.

Current Speaker of the House of Delegates, Doctor Richard E. Anonsen, practices at the Tyrol Clinic, Minneapolis. He is in family practice and is a diplomat in the American Board of Family Practice.

Doctor Anonsen was born in Willmar and received his undergraduate education at the University of Minnesota. In 1954, he received his M.D. degree from the University, then interned at Hennepin County General Hospital.

During World War II, he served in the Pacific with the U.S. Navy and Marine Corps.

He is a member of the Hennepin County Medical Society, American Medical Association, Alpha Omega Alpha and Academy of Family Practice. He is a past president of the Hennepin County Chapter of the Academy of Family Practice; past president and chairman of the board of directors of the Hennepin County Medical Society and the Foundation of Health Care Evaluation. He is past chief of staff of Eitel Hospital.

With the Association, Doctor Anonsen has been speaker of the house for two years. Prior to becoming speaker, he served as a member of the Committee on Medical Service and Subcommittee on Standards of Medical Care and as vice-speaker.

He has four daughters and likes water skiing, snow skiing and hunting.

James H. Kelly, M.D.

Doctor James H. Kelly has practiced in St. Cloud since 1958. Here he practices with five internists; serves on the staff of St. Cloud Hospital and serves on the consulting staff at St. Cloud VA Hospital.

Doctor Kelly graduated from St. Thomas College in 1944, and received his M.D. degree from the University of Minnesota in 1947. For seven years prior to his residency, he was in family practice in Wadena and St. Paul. He did graduate work at Ancker Hospital, St. Paul, and the VA Hospital, Minneapolis, completing his residency in 1958. He was board certified in internal medicine in 1962.

Doctor Kelly is a fellow in the American College of Physicians and the American College of Chest Physicians and is a member of the American College of Cardiology. He is a past president of the Minnesota Heart Association. Currently he represents the Minnesota State Medical Association on the Comprehensive Health Planning Advisory Council.

He has been a delegate from the Stearns-Benton County Medical Society for 10 years and has served on the MSMA Heart Committee and Committee on Rheumatic Diseases.

Doctor Kelly and his wife, June Elizabeth, have eight children. The family owns and operates a resort, Coppersmith Lodge, on Lake BelleTein near Park Rapids.

Vice-Speaker

James W. Halvorson, M.D.

For many years, Doctor James W. Halvorson, Zumbrota, has been an active member in the Minnesota State Medical Association. Besides membership of the Committees on Alcoholism and Drug Abuse; Mental Health; Automotive Injuries; and Interns, Residents and Medical Students, he has been a legislative contact physician for the Committee on Public Policy and MSMA vice president, 1971-72.

A past president of Goodhue County Medical Society, he serves as one of its delegates to the MSMA House of Delegates. He is on the Board of Editors of MINNESOTA MEDICINE.

Doctor Halvorson is a former member of the Minnesota State Board of Health and of the regional advisory group to the Northlands Regional Medical Program.

Known for his work combating alcoholism and in programs relating to the drinking driver, Doctor Halvorson was given the AAA Service to Motoring Award in 1972. He is vice president of the Minnesota Council on Alcohol Problems and serves on the Advisory Committee to the Hennepin County Alcohol Safety Action Project.

Doctor Halvorson is a native of Brainerd. He received his medical training at the University of Missouri and University of Minnesota and interned at St. Mary's Hospital, Duluth. He has been in family practice in Zumbrota for nearly 20 years and is a diplomat in the American Board of Family Practice.

Robert Hugh Monahan, M.D.

Doctor Robert Hugh Monahan, presently the vice-speaker of the House of Delegates, was born in International Falls. He received his B.S. degree, 1940, M.B. degree, 1942, and M.D. degree, 1943, from the University of Minnesota. He interned at Charles T. Miller Hospital, St. Paul, and completed his residency in ophthalmology in 1950 at the University of Minnesota. Doctor Monahan was a fellow in eye pathology at the Massachusetts Eye and Ear Infirmary and in Ophthalmology at Harvard Medical School. In 1951 he became a diplomat in the American Board of Ophthalmology.

In addition to being vice-speaker, Doctor Monahan is chairman of the Association Committee on Ophthalmology.

He has held a number of teaching appointments and currently is Clinical Professor, Department of Ophthalmology, University of Minnesota.

He is a member of the American and Minnesota Academies of Ophthalmology and Otolaryngology; American and Minnesota Associations of Ophthalmology; Pan American Ophthalmological Society; Pan American Eye Pathology Society; Midwest Eye Pathology Society; National and Minnesota Societies for the Prevention of Blindness; Georgiana Theobold Society (Midwest Eye Pathology Society) and the American Institute of Parliamentarians.

He has held numerous administrative positions including Director of Medical Education in Ophthalmology, Ancker Hospital; Chief of Staff, St. Paul-Ramsey Hospital and Medical Center; President, Minnesota Medical Alumni Association; President, Joint Commission on Allied Health Personnel in Ophthalmology; President, Minnesota Association of Ophthalmology and President, Minnesota Academy of Ophthalmology and Otolaryngology. Currently. he is president, Minnesota Association of Ophthalmology.

Doctor Monahan is a prolific writer on ophthalmic subjects and has published in many journals. He also has presented numerous papers before professional groups of ophthalmology.

May Is Our Turn

121st Annual Meeting

A candid conversation with the two men who are responsible for a major part of the annual meeting.

Dr. William E. Jacott,* a family physician, and a native of Duluth, has been practicing in Duluth since 1965. He is active in the community as well as in professional organizations. He is an active member of the Minnesota Chapter of the American Academy of Family Physicians and the St. Louis County Medical Society. Continuing Medical Education has long been one of his main interests and pursuits; he is presently a member of the faculty of the University of Minnesota Medical School at Duluth. Appointed as chairman of the Local Arrangements Committee by the St. Louis County Medical Society, Dr. Jacott is also a member of the Scientific Assembly Committee.

Dr. Robert D. Semsch† started practicing in Minneapolis in 1947, originally as a pediatrician, later, in 1970, devoting full time to his subspecialty, allergy. Prior to that he served two years as a captain in the Pacific theater and in Honolulu. Dr. Semsch has served on a number of committees of the Minnesota State Medical Association and as president of the Hennepin County Medical Society. He has made many contributions in the field of pediatrics, including working with allergies in children. He is a member of the American College of Allergists and a member of the American Academy of Pediatrics. Dr. Semsch is also active in his community. Long committed to and interested in Continuing Medical Education, he was nominated as chairman of the 1974 Scientific Assembly Committee.

The Editors:

Dr. Semsch, when you were approached in the autumn in regard to planning a scientific program, what was your first reaction?

Dr. Semsch:

Getting people together for one thing—there's plenty of physicians around who are interested and willing to help put together a two day scientific session, but you don't always know where and who they are. The Scientific Assembly Committee tries to keep in as close communication with the Local Arrangements Committee as possible, kind of the right hand knowing what the left hand is doing, and luckily, Dr. Jacott accepted an invitation to sit on the Scientific Assembly Committee. Once the list of committee members is complete, our first responsibility is to choose a theme for the program. Then the real work begins. Picking topics, finding speakers, making contacts to find out what our members want, and who wants to participate. A chairman needs good men who are willing to spend a lot of time on this project, and I feel very fortunate that I had such an able crew. With their help, a program has been assembled in record time, and it's good, too.

The Editors:

We have the same questions for you, Dr. Jacott; what was your reaction to being nominated as Local Arrangements Committee chairman, and what is involved?

Dr. Jacott:

We are enthusiastically looking forward to this Duluth meeting—speaking professionally and for the community. I'm happy to offer the Duluth Welcome Mat to all the physicians in this state. As for the work involved, it's mostly public relations and planning the social events. Dr. Semsch already mentioned that the Local Arrangement Committee and the Scientific Assembly Committee work together so there will be no conflicts in scheduling. Besides the bridge, golf and tennis tournaments, we take care of the arrangements for the President's Reception and the entertainment for the banquet.

The Editors:

We'd like to come back to the tournaments, Doctor, but first, Dr. Semsch, you seem to be quite pleased with the scientific program.

Dr. Semsch:

Yes, indeed, the program totals 13.5 hours, accredited by the American Medical Association. Of course, the AMA accreditation is mainly due to the superlative program Dr. Harley Racer produced in 1973. However, we have to keep up certain standards in order to retain it. The program is also acceptable for 13.5 prescribed hours

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*Chairman, Local Arrangements Committee.
†Chairman, Scientific Assembly Committee.

by the American Academy of Family Physicians. There aren't very many state medical associations around that have their programs accredited by both, so we are quite happy about it. Of course, only the evaluations will tell us if it was worthwhile to the people who attended it and that's the most important thing.

The Editors:

Is evaluation of the program by those attending it really important?

Dr. Semsch:

It is, for a variety of reasons. As you know, continuing medical education is a requirement of membership in the Minnesota State Medical Association, therefore, it is now the responsibility of the Association to provide meaningful programs in order for the physicians to acquire the credits they need. The evaluation form is the only way we will know whether we are meeting their needs. It will also give us some direction for future programs.

The Editors:

What about the institution of a registration fee this year of $10.00 for members and $25.00 for non-members?

Dr. Semsch:

The Minnesota State Medical Association has a commitment to provide the best possible programs for its members—this costs money, and we are using the same method to increase the budget that all other organizations use.

Dr. Jacott:

I wholeheartedly support Dr. Semsch's statements in regard to the evaluation form and the charging of a fee. The Minnesota Academy of Family Physicians has been using a similar system for two years. Tuition for most programs is a lot more than $10.00 or $25.00; economically it's a very sound decision to make.

The Editors:

Dr. Jacott, we understand that there are a few changes this year in some of the formats.

Dr. Jacott:

Yes, we're adding a little variety to the President's Reception—there'll be wine tasting as well as a bar for the uninitiates. We've brought back the bridge tournament, and picked the Moorish Room at the Hotel Duluth for it. It's a perfect room for this type of activity. The golf tournament will be at Northland Country Club again, and the tennis tournament will be at the new Duluth Indoor Tennis Club. With our natural air conditioning, I'm sure a lot of players will find the latter club pretty nifty. We're having a joint golf and tennis awards dinner which is also a slight departure from tradition.

The Editors:

It sounds like the Local Arrangements Committee has been very busy this winter.

Dr. Jacott:

We certainly have—there'll also be a special bus service between the major hotels and the arena.

The Editors:

Dr. Semsch, we understand that there will be some changes in the Scientific Assembly Committee next year. Can you tell us about it?

Dr. Semsch:

Well, nothing will be decided until the House meets during the annual meeting, but the Medical Education Committee and the Scientific Assembly Committee have recommended that the Scientific Assembly Committee becomes a permanent subcommittee of the Medical Education Committee. Our reason here is based on the continuing medical education requirement as well—there has to be continuity in the committee and what it does. It's nearly impossible when the whole committee is disbanded after the annual meeting, and then a completely new one is put together the next fall.

The Editors:

We see your point, thank you Doctor. Dr. Jacott, the social highlight of the meeting is the banquet—how are the plans coming?

Dr. Jacott:

The banquet will be held in the ballroom of the Hotel Duluth. We promise great entertainment and a really fine orchestra for dancing. What enhances the banquet is the presentation of the Distinguished Service Award and the President's Awards. There are twenty-one newcomers to the Fifty Club, and we're happy to hear that most of them will be there.

The Editors:

Thank you both, Doctors, for giving us this opportunity to hear what it's like behind the scenes.

Dr. Jacott:

We certainly appreciate this chance to inform the physicians in this state about the annual meeting. We're really looking forward to it and we hope they are too.

We need you.

If you can spend some time, even a few hours, with someone who needs a hand, not a handout, call your local Voluntary Action Center. Or write to "Volunteer," Washington, D.C. 20013.
The National Center for Voluntary Action.

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(Continued to Page 339)

X-ray Conference

Chest Xray after Auto Accident

The patient,* a 36-year-old female, presented with a chest radiograph showing a very high and large aortic knob (Figure 1, arrow) that has increased in size since six years ago (Figure 2). On physical examination the only finding was a grade II/VI systolic ejection murmur which had been present for six years. The patient did have an auto accident in the intervening period, but there was thought to be no severe chest trauma.

What is your diagnosis?

---

*Case courtesy of Dr. T. E. Johnson, St. Paul.

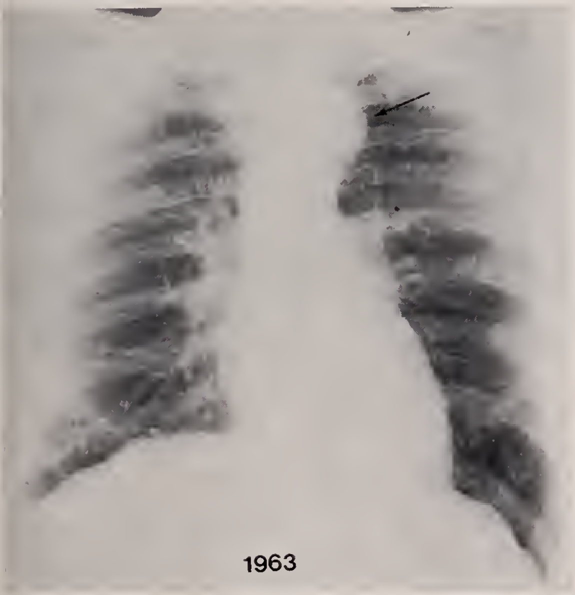

Figure 1

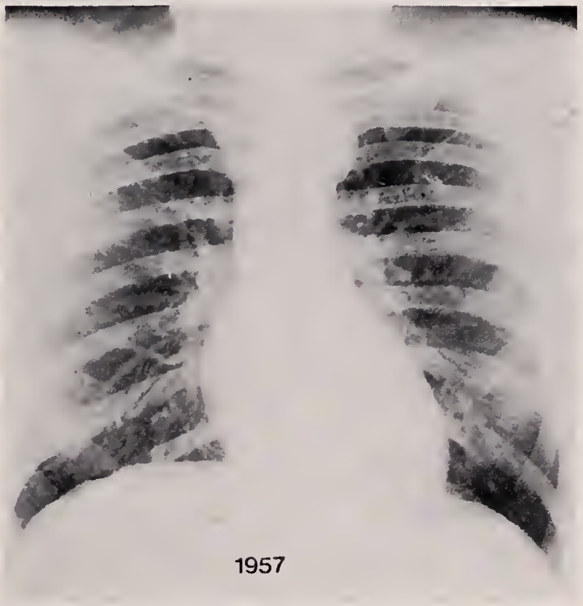

Figure 2

Diagnosis: Pseudocoarctation of the aorta.

Your differential diagnosis probably included aortic aneurysm (posttraumatic or dissecting) and mediastinal tumor. The diagnosis of pseudocoarctation of the aorta was established by aortography.

Note on the aortograms (Figures 3, 4) the kinking of the aorta (Figure 4, large arrow) the anomalous origin of the right subclavian artery (Figures 3, 4, arrowhead), and the dilated proximal few centimeters of the left subclavian artery (Figure 4, small arrow). The enlarged aortic knob (Figure 3, arrows) is actually a confluence of the high aortic arch, the kinked descending aorta, and the dilated origin of the left subclavian.

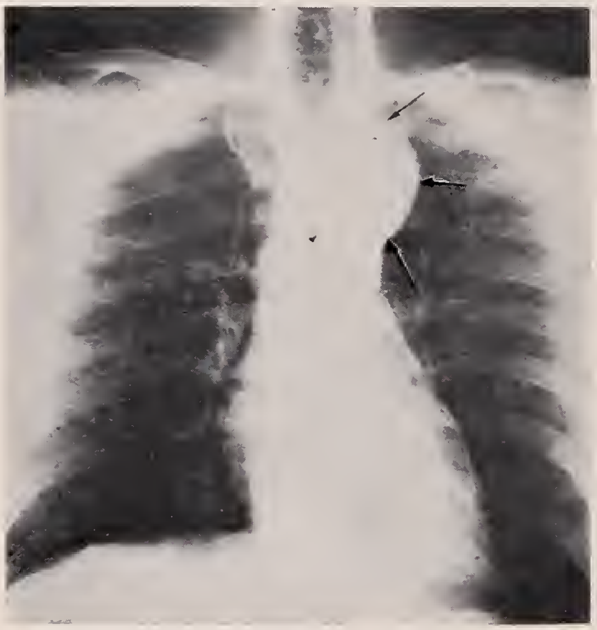

Figure 3

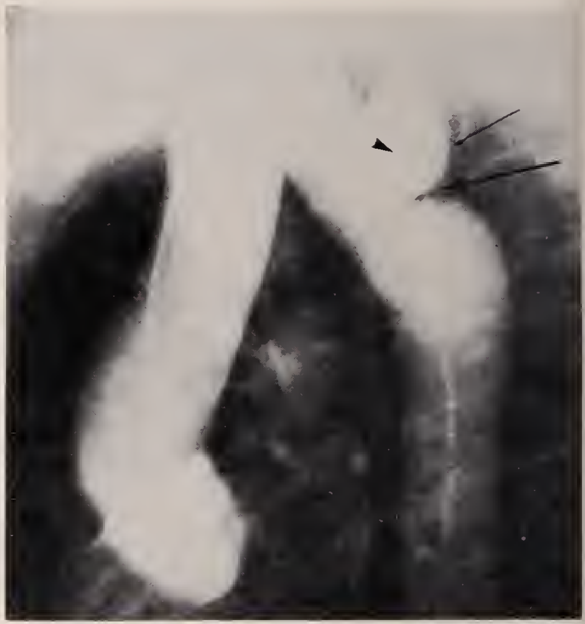

Figure 4

Comment

Pseudocoarctation is an uncommon entity with only about 100 cases having been reported to date. The term "pseudocoarctation" was first suggested by Dotter and Steinberg[1] in 1952. Other authors have suggested the terms "kinking"[2] or "buckling"[3] of the aorta and "subclinical coarctation."[4] The entity is important to recognize because its confusion with aortic aneurysm, dissection, or mediastinal tumor might lead to an unnecessary thoracotomy.

In pseudocoarctation, the arch is elongated, rising higher in the mediastinum than normal. Then the aorta arches more sharply forward, downward, and to the right as its descends. The kink usually occurs at the aortic isthmus often causing a systolic ejection murmur. Distal to the kink, there is a small dilatation.

The radiographic findings reflect the above description. Oftentimes, a double density is seen in the area of the aortic knob. The top density represents the knob. The bottom density represents the buckled descending aorta. In this case, these densities blend with one another (Figure 1). In the lateral view, anterior compression and displacement of the esophagus by the kinked aorta is sometimes seen with the barium swallow.[5]

The development of pseudocoarctation probably occurs during embryogenesis.[2,6] To support this etiology, several associated congenital heart diseases have been reported.[7] Among them are patent ductus arteriosus, bicuspid aortic valve, atrial septal defect, ventricular septal defect, and aortic stenosis.

Pseudocoarctation appears to be a variant of true coarctation with both having similar photomicrographic appearances.[8] Pseudocoarctation, however, differs mainly by an absence of sufficient narrowing to cause a pressure gradient across the constriction. Thus, patients with pseudocoarctation do not have collateral circulation, rib notching, lag of femoral pulse, or pressure differences between upper and lower extremities. The definitive diagnosis is dependent on angiography. This reveals an area of kinking and evidence that there is no significant pressure gradient across the area.

Differentiation of pseudocoarctation and true coarctation may be more difficult than merely demonstrating that there is no pressure gradient across the area of narrowing. Gupta and Wiggers[9] have shown that no pressure gradient occurs until the cross sectional area is reduced to 40% of the normal and no *significant* pressure gradient is seen until the cross sectional area is reduced to 25% of the normal. However, laminar flow is lost at 78% of the normal cross sectional area[4] leading to turbulence of flow (murmur) and possibly post-stenotic dilatation.

In light of the above information, some authors have suggested surgical resection of the pseudocoarctation because of the potential development of aneurysmal dilatation. Gay and Young[10] reported the death of one of their patients with pseudocoarctation from a ruptured aortic aneurysm. Prian[11] reported a case in 1972 which had been followed for 13 years with serial chest radiographs every six months who suddenly developed a large aneurysm. Surgery was successful in this case. A special concern as the patient gets older is the natural elongating effect on the aorta that hypertension, atherosclerosis, and kyphosis produce leading possibly to further buckling of the aorta and aneurysmal dilatation. The surgical approach is controversial. Indeed, there are numerous reports of unnecessary surgery on pseudocoarctations which were thought to be superior mediastinal tumors[2,3]; mediastinal Hodgkin's lymphoma[12]; and aortic aneurysm.[13]

Pseudocoarctation is usually benign and simulates other left superior mediastinal masses. The reported cases of aneurysm distal to the point of narrowing point to the need for frequent chest radiographs as the patient ages.

Dennis Sternke
Phase D Medical Student
University of Minnesota

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Society President's Letter

Minnesota Society of Internal Medicine

The Minnesota Society of Internal Medicine has as its aim the exchange of clinical and scientific information between its members as well as all physician guests who attend its two meetings a year. Over the years the Society has taken no action relating to economic or political problems of the profession. These problems have been well handled by the Minnesota State Medical Society, the Association of Minnesota Internists as well as several of the other specialty Societies.

With the steady encroachment of government upon the practice of medicine and the apparent inevitable regimentation of the medical profession, all physicians and all medical societies must take an active and productive part in shaping the future of our medical life. One step that our Society has taken is to support the Committee on Medical Education of the State Medical Association on its leadership in promoting continuing medical education as a basis for membership in the Association. Our Society has prepared suggested acceptable minimal requirements of medical education appropriate for members of our Society.

Legislators in various states have discussed possible legislation to require physicians to show proof of continuing medical education. Fortunately no such legislation has been yet set up in any of the States. We as physicians must take the responsibility and leadership in this field and set up our own requirements of medical education and enforce them or government will do it for us.

But not only must all medical organizations take a more active part in economic, social and political problems of our country but all physicians must take a personal interest and actively participate in the non-medical community life of society in order to "shape the things to come."

Delmar R. Gillespie, M.D.
President
Minnesota Society of Internal Medicine

The Doctor's Image of Himself*

C. DWIGHT TOWNES, JR., M.D.†

THE EXPECTATIONS and demands we put on ourselves and society puts on physicians are heavy, conflicting, and stressful. The self criticism and public criticism laid on the physician who doesn't measure up to these expectations is heavy too. We have been reading more and more lately about the vulnerabilities of physicians to drug and alcohol addiction, bad marriages, divorce, depression, and suicide. It is good to get these things out in the open; maybe we are not aware of our vulnerabilities. Maybe we don't want to be aware of them. We want to believe, "It won't happen to me." Satchel Paige said, "Don't ever look back, something might be catching up with you." By looking at what has happened to some other physicians, and at the situation of physicians in general, we may be able to see what we can do to make sure these things don't happen to us.

The doctor's psychologic life style, his self image, affects every relationship he has—with himself, his wife, his children, and his community. How does he like *himself?* How can the compulsive personality it takes to get through medical school ever be satisfied with himself? He demands perfection and perfection is impossible. The implied requirements for charisma and omniscience lead him to believe he should try to play God, and some of his patients may want to put him in that position, but he cannot always hide his feet of clay. It is not that most doctors don't think highly enough of themselves. The problem is the demands they put on themselves because of too strong a sense of responsibility. Personality studies have shown that physicians who became addicted to narcotics were emotionally immature, had a history of chronic disturbance in their close relationships, were subject to frequent psychosomatic difficulties in childhood, showed a basic insecurity, and had excessively high, unrealistic aspirations. "With purity and holiness I will pass my life and practice my art." The physician's need to be loved, to be adulated, to feel superior is greater than that of most other people. That may be why he chooses what would be called a God-given profession.

Most physicians are oldest or only children. This place in the birth order usually influences a child to identify with parental authority as a defense against the threat of dethronement by a second child; for the only child as a defense against the world. First children tend to be more serious minded, more conforming, more compulsive, authoritarian and successful. Not necessarily happier or more satisfied with themselves, however.

Compulsiveness often leads to frustration and depression, and these are forerunners of suicide. For the general population the suicide rate is about 10.5/100,000. The range reported for physicians is between 12/100,000 for radiologists and 70/100,000 for psychiatrists. 100 physicians commit suicide each year in the U.S. Most are under age 50. Drugs are the most used means. All reports relate the frequency of suicide to alcoholism and drug addiction.

The die is cast for the problems of the so-called "deviant" physician in childhood. The definition of the deviant and what to do about him in medical school and practice were discussed by a panel at the Congress of Medical Education meeting in January, 1973. People in the audience and on the panel used the term for anyone from long hair to radical bigot. A matron met a sorority sister one day and asked the usual question about children. Her friend replied dismally that her daughters were fine, but her son was a practicing homosexual. "How wonderful!" gushed the first lady, "Where is his office?"

In a fascinating progressive study of 126 people started when they were sophomores in college 30 years ago, Dr. Vaillant's group found that the ones who went into medicine, especially those involved in direct patient care, were more likely to have relatively poor marriages, to use alcohol and drugs heavily, and to obtain psychotherapy. (This last tendency is in contrast to what Duffy and Litin found in their study of the emotional health of physicians in which they state, "he is extremely resistant to admitting his psychopathology and accepting treatment. The physician fears a psychiatric diagnosis. There is a stigma associated with it. The ramifications extend far—state medical societies, insurance companies, and federal agencies are quick to regard as poor risks those physicians who have had emotional disturbances.")

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*Presented at the Annual Meeting of the Minnesota State Medical Association, May 25, 1973, in Minneapolis.

†Family Physician, Assistant Professor, Hennepin County General Hospital, Minneapolis.

Vaillant found that physicians' difficulties were strongly associated with life adjustment before medical school, particularly with unhappy childhoods. When asked if medical school admission committees should screen out everyone with an unhappy childhood. Dr. Vaillant said, "No, these people make very altruistic physicians because of their strong urge to give to others the care they did not receive in their own childhoods. Of course, they do need support and guidance because they tend to take out anger and frustration on themselves, and to be hypochondriacal. So it is not the type of childhood you had or the stresses of your profession, but what you do with them that makes or breaks you. When interviewed, the controls would say, "There is very little wrong with me." The physicians would say, "There is a lot wrong with me, but I will not inconvenience anyone else."

What about *medical marriages?* "A doctor is not a good husband. He is gone all the time. His profession is his jealous mistress. Patients always come before family. You can never count on him. He is woefully ignorant and hung-up about sex. He is demanding and dictatorial, expects his wife to obey orders like nurses do. You can't argue with a doctor!"

I doubt if any of you have the September, 1969 McCall's at home, but my wife saved an article from it entitled "Don't Marry a Doctor!" Those were quotes from it. It is actually a well-researched article. All the interviewers said they would not want their daughters to marry doctors.

While their divorce rate is about the same as that of other professionals, Census Bureau figures show that doctors rank way above them in the category "Spouse absent from the home," meaning a formal or informal separation.

Statistics reveal today's doctor as a paragon of success in all but his personal life. M.D.'s are the largest occupational-group buyers of Lincoln Continentals. Seventy-two percent of them own two cars, and the second is a Detroit built station wagon. Forty-one percent own a third car, a fast European sports model. He marries at age 26, compared to age 23 for most males, and produces a minimum of three children. His most frequent domestic complaint is that his wife is extravagant. Other men mostly complain that their wives are ill-tempered.

He is intelligent but not intellectual: the average physician reads fewer than four non-medical books a year, and 40% read fewer than two a year. His favorite sports are golf, tennis, handball and perfunctory six-lengths-of-the-pool swimming. These are conscientious physical exercises rather than social events, and seldom include his family. In spite of this he weighs 12 pounds more than the average American male. Dublin has found that the rate of death from coronary artery disease is 80% higher among doctors in the age group between 45 and 65 than among the general population this age.

One physician's wife said, "Jim is basically a very decent person, but he finds it difficult to behave like one. Marrying a doctor is like marrying a man who has spent six or eight years in a very good mental institution. That's what medical school is! You send nice boys to med school and they are never the same again. They get their brains washed out there. All they are taught is how to cope with illness, nothing at all about love and consideration for human beings."

Does he know how to cope with his *children?* The physician is usually a very possessive and directive father. In many medical households Papa cracks the whip. Often the household schedule has to turn on the axis of his professional needs. This may lead to dominated children. The child who chafes may react in one of three ways: (1) become meek and fearful, (2) withdraw into a world of make-believe where things are better or (3) become sullen. Dr. S. J. Griboff is convinced that a doctor can best learn to be sensitive to his patients' feelings and values in the closest of human relationships the family; that a better father and husband is a better doctor.

The physician father may not only be too authoritative, but he may also be a less than ideal model. Physicians as a class have the highest incidence of narcotics addiction, ranging from 1/100 to 1/400. Demerol is the most frequent drug abused. Thirty to 100 times as many physicians suffer from drug dependency as does the general population. Drug addiction is an occupational hazard because of the easy access the physician has. Also he is trained and dedicated to the use of medicine to cure or ease the ills of his patient, why not his own? Alcoholism is also a frequent problem for the physician. He uses alcohol for medicinal purposes too, as a tranquilizer. Many of us don't know enough about early stage alcoholism or prescription drug addiction to recognize them in our patients or in ourselves.

The physician is often a *community* leader. The same sense of responsibility and compulsiveness that got him into and through med school get him into all sorts of projects—committees, boards, fund drives, health officer, volunteer in free clinics, indispensable member of abortion discussion panels and so on and so forth. The AMA and other medical organizations exhort him to GET INVOLVED; to exert his political punch. So he does, and he soon spreads himself too thin, gets more exhausted and irritable and frustrated.

The most prominent early sign of emotional disturbance in physicians is the manner of living a hurried existence, with a gradually developing chaotic everyday life regarding his office hours, appointments, eating and sleeping habits and family responsibility.

What can we do to prevent emotional disturbance, depression, suicide, to maintain our marriages, the love and health of our children, and keep our community responsibilities within reason? If we had a happy childhood we don't have too much to worry about—the odds that we will have trouble are down to those of the average American. If we had an unhappy childhood, it is imperative that we get some help. In either case, here are some suggestions:

A. For one thing, we can get a checkup once a year—mental as well as physical.

B. Marriage checkups also are recommended and offered.

C. We might even want to try to change, with help, our Life Style, learn to communicate without giving orders, to relax without drugs or alcohol.

D. When our self image flags, we can recall this quotation from Robert Louis Stevenson, "There are men and classes of men that stand above the common herd; the soldier, the sailor, and the shepherd not unfrequently; the artist rarely; rarelier still, the clergyman; the physician almost as a rule. He is the flower (such as it is) of our civilization; and when that stage of man is done with, and only remembered to be marveled at in history, he will be thought to have shared as little as any in the defects of the period, and most notably exhibited the virtues of the race. Generosity he has, such as is possible to those who practice an art, never to those who drive a trade; discretion, tested by a hundred secrets; tact, tried in a thousand embarrassments; and what are more important, Heraclean cheerfulness and courage. So it is that he brings air and cheer into the sickroom, and often enough, though not so often as he wishes, brings healing."

E. We can help each other by acting on our ethical responsibility (as reiterated by the AMA Board of Trustees in Cincinnati last fall) to recognize a colleague's inability to practice medicine adequately because of physical or mental illness, including alcoholism or drug dependence, to attempt to persuade him to seek help, and if that fails, refer the problem to his hospital staff or medical society.

F. Since most of us still, in spite of what Dr. Vaillant found, hesitate to seek help from "shrinks", here is a list of some ways to get the benefits of psychotherapy without going to a psychiatrist:

1. Read books—not psychiatric texts, they're too depressing—but good "Popular" psychology like, *I'm OK, You're OK, Open Marriage, Psychocybernetics.* Biographies of physicians help us feel better about our own lives; *One Life* by Christiaan Barnard, *The Making of a Surgeon* by William Nolan.
2. Ventilate to your wife, and listen to her. Sit down with her at least once a year and review your goals and priorities.
3. Play with your children. Ask one of them to rub your neck when you have a headache.
4. Attend courses and lectures on psychotherapeutic topics, including human sexuality.
5. Have at least one partner, and hold weekly meetings of the partnership or corporation to discuss interpersonal relationship items as well as management and

medical problems.

6. Get involved in a church, but be sure it is one that emphasizes grace not guilt and fear.

7. Join or organize with your wife a small discussion group with couples and meet every month for the rest of your lives to discuss anything the group wants to—books, plays, movies, marriage, children, in-laws, religion, sex, death. No leader, just let leadership be rotated or come naturally. Let the group be a place where you can let your mind down.

8. Meet with your office staff often for ventilation both ways and for studying participatory management and democratic problem solving with the aid of good texts like *The Managerial Grid.*

9. Take a study group course with your wife in Transactional Analysis or Parent Effectiveness or Couples Communication or Adlerian Child Rearing. Dreikurs' book *Children the Challenge* is the most encouraging thing I've found for parents.

10. Do some psychotherapy in your practice, preferably with more than one patient and more than one therapist present. It works both ways.

11. Resign from all committees, or at least attend few irregularly.

12. Attend Executive Power Seminars and such where businessmen learn how to think positively.

13. You might even try T-grouping; it could teach you to be less defensive.

14. Say your self affirmations and/or pray daily.

15. Take a family trip once or twice a year.

16. The best way to get some good transcendental meditation is to go fishing. Sometimes it even helps your self image.

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A new method utilizing the intravenous injection of tetrabromphenolphthalein defines a distinct shadow of the gallbladder as obtained on exposure to the x-ray. Shadows have been obtained on all patients who presumably have normal gallbladders. It is difficult to obtain a shadow of a pathologic gallbladder. We believe that this fact will be almost as much of an aid in diagnosis as a good shadow since we feel that virtually all normal gallbladders can be made to cast a shadow if proper methods are used.*

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*Evarts Graham and Warren Cole. JAMA 82:613, 1924.

Family Practitioners in Minnesota

Need and Distribution

JOHN W. McCONNELL, M.D.*

As American medicine has developed and expanded over the past 200 years, Minnesota has established itself with an estimated 1293 primary care physicians.[1] What does this mean to the citizens of this state? Is there a need for doctors over and above the presently available supply? Some interesting figures and facts bearing upon such questions have come to light during a search conducted recently by the Department of Family Practice and Community Health. The report of the Department published in this journal alluded to these findings.[2] The present paper centers upon a more detailed discussion of the subject.

The vast majority of primary care is delivered by the group termed family physicians in the Northlands Regional Medical Surveys.[1] This group is composed of General Practitioners or Family Practitioners and certain members of the specialties of Internal Medicine and Pediatrics. The distinction between the Family Physician group, as designated by the Northlands Survey, and the Family Practitioner, the title chosen by the members of the newest medical specialty group in the AMA, must be kept in mind. How great a contribution is provided by the internists and pediatricians included in the Family Physicians is a matter of conjecture. In most instances, the dominant, traditional role of the specialist has been the delivery of secondary or tertiary care. A number of specialists are delivering primary care, however. The question remains as to what pro-

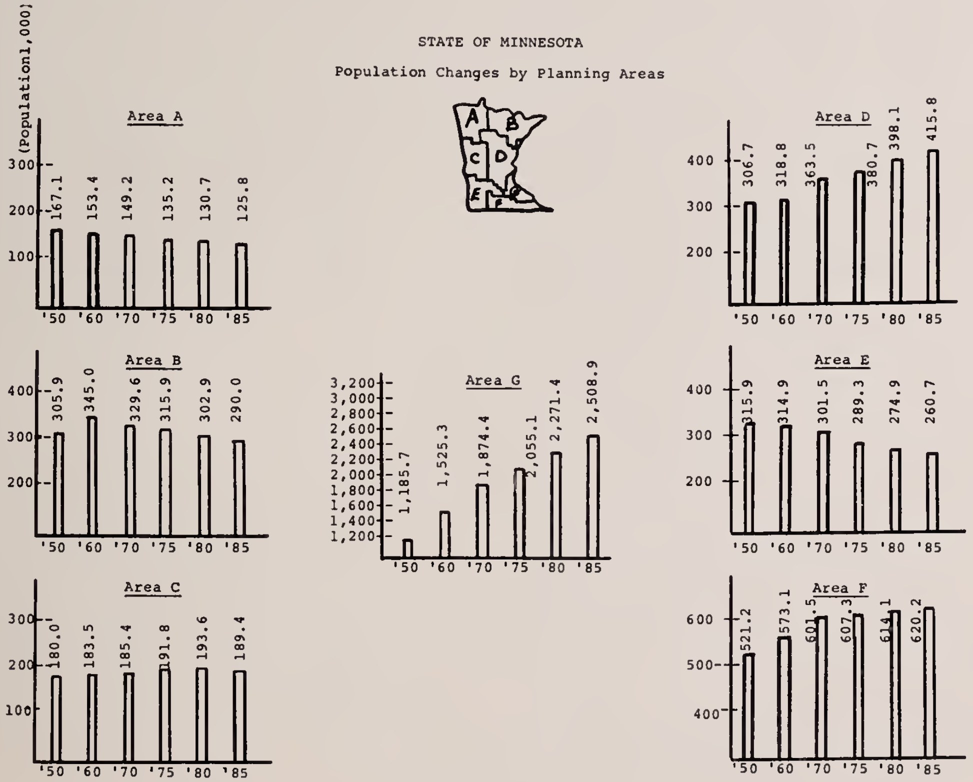

Figure 1

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*Assistant Professor, Department of Family Practice and Community Health, University of Minnesota.

portion of their time is devoted to primary care and the cost of the care provided by these specialists.

Distribution of population and physicians is also a consideration which plays a part in determining the answers to the questions posed above. The nature of the specialists' training, for example, produces a physician who is well equipped to deal with complex or obscure problems in a rather narrow medical field. He is taught to use all of the most complicated laboratory and therapeutic aids available and he may deal with patients in a relatively limited age range. Because of his interests and skills, he tends to locate in areas where special facilities are near at hand. In addition, the GP-FP population has shown some interesting changes in location in recent years.

The present study of general population distribution, doctor distribution, doctor work output and cost of medical care is based upon a variety of reports and statistical surveys. From the U.S. Census Survey of 1970[3] and the Northlands Regional Medical Report[1] of that same period, have come the majority of the figures concerning the numbers and distribution of population and doctors. The AMA Survey of Medical Practice[4] has furnished an estimate of nationwide physician work load, practice time and medical costs and the HEW Survey on numbers of patient visits to physicians yearly[5] has been most helpful in our search for some answers to our questions.

Figure 1 shows the changes in population distribution throughout the state and the location of the Minnesota Health Planning Regions.[1] The information presented covers past census surveys and includes projected population trends based on the available information.[3] It might be noted that, if the present trend continues, the rural regions are expected to have a gradual decrease in population and the more urban areas a rapid increase in inhabitants over the next 15 years. Overall, however, one might predict a general population increase in the state as is shown in Figure 2.

Figure 3 illustrates the family physician population of these various regions in terms of physicians/100,000 population in 1970. In addition, the relative numbers of general practitioners, internists and pediatricians are represented. With only a brief look at this Figure, one can see that the highest concentration of specialists reportedly delivering primary care is in areas in which larger medical complexes are located. The lines across the upper portions of the graphs, entitled average, urban and rural, represent the national average of general practitioners per 100,000 population.[4] No such ideal ratio for family physicians has been estimated on a realistic basis.

A closer look at the graphs reveals some rather interesting findings. In Area A, for example, the primary care physician population is decreasing at an even more rapid rate than is the general population in this area. Area B, on the other hand, appears to be recovering somewhat from the relative decrease in primary care physicians which it experienced in 1960. This is partly due to an influx of specialists engaging in primary care. It is also changed by the population increase in the 1960's as shown in Figure 1.

Area D is unique in the state due to its higher urban population concentration and relatively rapid population increase as compared to the other planning areas. Here the physician/population ratio has maintained its own, although only barely, due mainly to a relatively rapid increase in the numbers of internists and pediatricians there who are devoting time to primary care delivery. The same observations may be made for Area G as well.

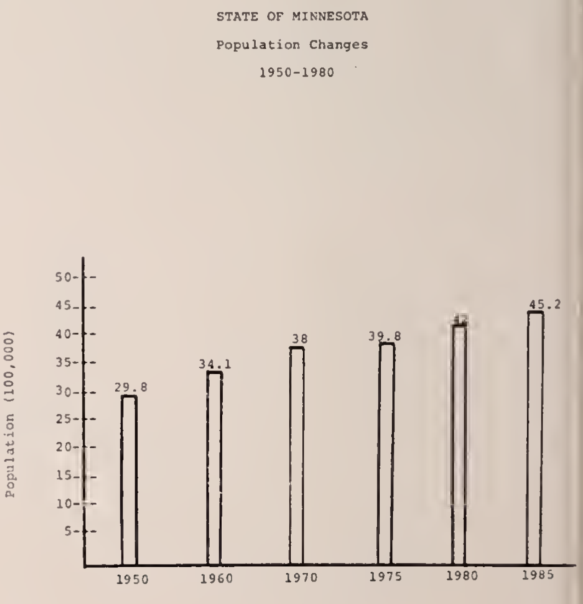

Figure 2

Turning to Area C, a decrease in both population and physicians is easily noted. On the other hand in Area E the population decrease coupled with a relatively steady doctor population has led to a relative increase in the doctor/population ratio. The only really positive increase in both population and primary physician/population ratio in the state has occurred in Planning Area F. Overall, a gravitation of both primary physicians and population to the more heavily populated regions of the state has taken place over the past twenty years. The reasons for this phenomenon, whether economic, educational or cultural are not a primary focus of this paper but

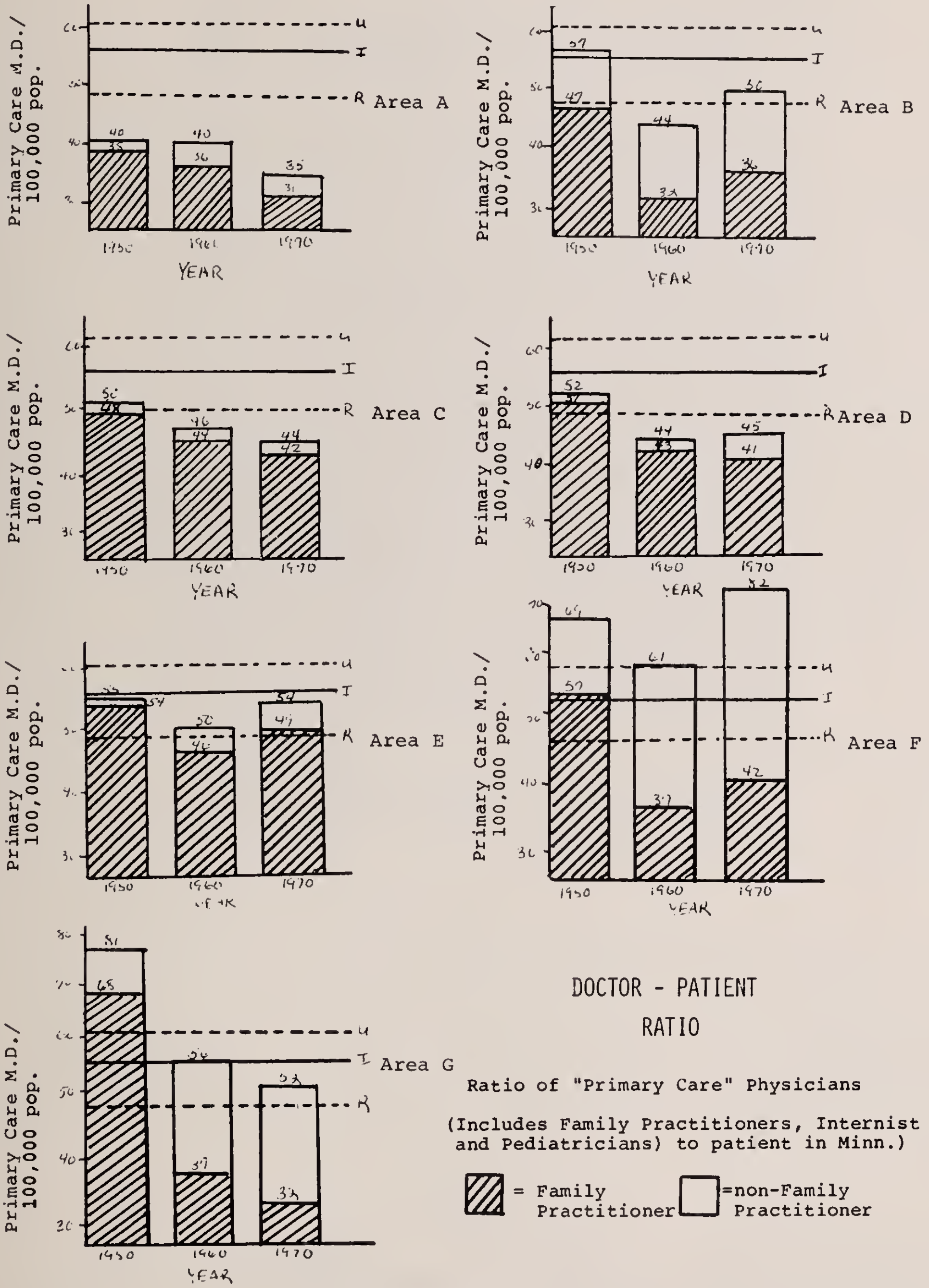

Figure 3

would bear investigation.

Regarding average work output, the specialist sees fewer patients per week and works fewer weeks per year than the general practitioner[4] (Table 1). This conclusion is based on the national figures published by the AMA 1971 and the U.S. Vital Statistics Surveys.

TABLE 1

	patient/week		week/year		patient/year
Internal Medicine	127.2	×	47.9	=	6092.88
Pediatrics	146.5	×	48.1	=	7046.65
General Practice	167.0	×	48.3	=	8066.10

From the above table, it can be concluded that the average general practitioner sees and treats 1.22 times as many patients per year as does his specialist co-worker. The number of visits to the specialist which are of primary care nature is, however, unknown.

The cost of medical care is an issue related to that of need for more primary care physicians and is of relatively great importance to today's consumers and politicians. National averages concerning costs of office calls to the patient are to be found in a 1968 survey of medical costs[5] and are shown in Table 2. By means of these figures, it is estimated that the cost of primary care would have been several millions of dollars higher in Minnesota in 1970 if delivered entirely by specialists.

TABLE 2

	Initial office visit	Follow up visit
Internal Medicine	$16.58	$8.57
Pediatrics	9.48	6.70
General Practice	7.83	5.84

4.5 patient visits/year average 4.8 M (Minn 1970) population by average cost/visits.

With all of the above in mind, let us proceed to some conclusions about medical needs and trends in the state at the present time.

First, it appears that while the total numbers of primary care physicians in the state seem great, the physician/patient ratio is gradually falling well below the national average. Second, although there has been a gradual shift in the population from the more rural to urban areas, the doctor movement to the cities is proceeding at an even more rapid rate than is the population movement.

Third, the present tendency to shift more primary care responsibilities to the specialist would require even larger numbers of physicians to be trained in the medical school than are being educated at present. These primary care delivery specialists would then need to be persuaded to settle and practice in the more rural areas of the state if the growing patient demand for care is to be satisfied. Even if such an attempt is made, the population growth may put grave stresses upon our specialist colleagues' ability to cope with the demands.

Last, but not least, the cost of medical care will become a more significant problem if the present trends are allowed to continue. This is of concern not only to the members of the medical profession but also to the legislators and citizens generally. We must give it proper attention.

Thus, the population of this state is growing, with an increasing tendency to urban concentration. The number of doctors practicing in this state has remained approximately the same, but they have tended to locate more and more in larger cities. The size of the Family Practitioner group has decreased and the cost of medical care increased. If the present concern about right to adequate medical care is an indicator, then the demand for primary care physicians will probably increase. Estimating future needs for the number of doctors to be trained depends on a variety of factors. Among these are the numbers of doctors leaving practice because of death, retirement, and change of specialty. Accurate assessment of these aspects of medical practice is needed before any realistic conclusions can be reached. Our Department is applying itself to the determination of such variables.

Acknowledgment

The author would like to express his appreciation to Eugene V. Lenarz for his comments on the organizatio and style of the article.

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Iaybe the patient's self-diagnois is right. He could have hay ever. But that bright red nasal nucosa, along with the thick disharge and excoriation around he nares, strongly suggests that he main problem is a cold. Hay ever or another form of allergic hinitis may or may not be an nderlying factor.

If a complete history and examination rule out allergic rhinitis, the long-term outlook will be a lot more favorable than his own "diagnosis" would have indicated.

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Ⓒ III Phenaphen with Codeine is now classified in Schedule III, Controlled Substances Act of 1970. Available on written or oral prescription and may be refilled 5 times within 6 months, unless restricted by state law.

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The Use of Micropore Filters

In the Administration of Intravenous Fluids

RODGER BUNKER,* CHERI JOHNSON† and MARY PRICE, M.D.‡

NORMAL SALINE, with and without inulin and odium hippurate, is used intravenously to test r renal clearance in the Department of Physical Medicine, University of Minnesota, and the Renal Function Laboratory of the Sister Kenny Institute.

Method

Since January 24, 1973, micropore filters[#] with pore size of 0.5 micron, have been inserted into he intravenous administration system just proximal to the intravenous needle for the purpose of emoving foreign particles from the solutions.

The testing solutions are prepared from commercially supplied sterile normal saline, sterile 0 gm % sodium aminohippurate and sterile 0 gm % purified inulin.

Visual Inspection

Before preparing the testing solution, the saline bottles and the ampules of sodium hippurate and nulin solution are inspected by individuals with good vision by holding them in front of an illuminated x-ray viewing box and scrutinizing them for foreign substances such as particles or fibers. Containers in which such contaminants are visible are discarded. During the past year the number of contaminated containers has increased substantially. When the micropore filters became available they were used as an added safety factor. Visually screening the containers for gross contaminants was continued as in the past.

To assess the practicality of using such filters, the last thirteen filters used as well as two unused filters were inspected with the unaided eye as well as with magnification of either 30x or 100x (Table).

No foreign particles were observed in the control filters.

One of six micropore filters used in the administration of 500 ml of saline, was found when examined by the unaided eye to have one dark particle on its surface. On six of six filters, examined with 100x magnification, were found multiple particles while four of the six had filtered out fibers of varying length.

Of seven filters used in the administration of 750 ml of saline, sodium hippurate and inulin in varying concentrations, four revealed particulate material and one a fiber visible to the unaided eye. With 30x magnification seven of seven contained particles and three of seven, fibrous material.

The foreign particles were estimated to be three to fourteen micra in diameter (a red cell is 7.5 micra in diameter). The single or multi-filamentous fibers were up to 2 cm in length.

TABLE
Contaminants Recovered from Intravenous Filters

		Unaided Eye		Magnified 30x		Magnified 100x	
	N	P	F	P	F	P	F
Control Filters	1	0	0	....	..	0	0
	2	0	0	....	..	0	0
Saline Filters	1	1	0	....	..	7	5
	2	0	0	....	..	9	2
	3	0	0	....	..	15	3
	4	0	0	....	..	16	2
	5	0	0	....	..	5	0
	6	0	0	....	..	10	0
PAH, inulin and saline filters	1	0	0	5	0	....	..
	2	2	0	7	0	....	..
	3	0	1	3	1	....	..
	4	3	0	12	3	....	..
	5	0	0	4	0	....	..
	6	2	0	8	2	....	..
	7	3	0	5	0	....	..

N = Number
P = Particles
F = Fibers.

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This research was supported in part by Research and Training Grant No. 2 from the Social and Rehabilitation Services.

[#] Travenol Plexitron extension set with Final Filter.

Conclusion

These findings indicate the need for better quality control in the manufacture of injectables. Until this can be accomplished, the use of a micropore final filter is a justifiable addition to the apparatus used in administering intravenous infusions.

Such censures our mistaking audience make,
That 't is almost grown scandalous to take!
They talk of fevers that infect the brains,
But nonsense is the new disease that reigns.
Weak stomachs, with a long disease oppres'd,
Cannot the cordials of strong wit digest.
Therefore thin nourishment of farce ye choose,
Decoctions of a barley-water Muse:
A meal of tragedy would make ye sick,
Unless it were a very tender chick.
Some scenes in sippets would be worth our time;
Those would go down; some love that's poach'd in rhyme.*

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*John Dryden: Prologue to 'The Loyal General.' 11. 18-29. 1679.

University of Minnesota Continuing Education Course

The Department of Surgery of the University of Minnesota announces its annual symposium in Surgery: "Surgery of the Liver, Biliary Tract, and Pancreas," May 29 through June 1, 1974 at the Leamington Hotel in downtown Minneapolis. This program is designed primarily for surgeons and is presented under the direction of Doctors John S. Najarian and John P. Delaney of the University of Minnesota Medical School. Guest faculty members will include: H. Joachim Burhenne, Ben Eiseman, Marvin L. Gliedman, John M. Howard, Frank G. Moody, Hans Popper, Seymour Schwartz, Sheila Sherlock, Rodney Smith, Thomas E. Starzl, W. Dean Warren, Thomas T. White, and Robert M. Zollinger. Further information contact: Dr. John P. Delaney, Box 89, University of Minnesota Hospitals, Minneapolis, Minnesota 55455 or by calling (612) 373-8807.

Cover Photo

"Spring at Como Park"

Dr. Robert O. Fisch took the cover photograph at the Spring Flower Exhibit at Como Park in March, 1972. He told the editors that he suggests everyone who has an opportunity should see this exhibit as it is a panorama of color and beautiful flowers.

Dr. Fisch is an Associate Professor in the Department of Pediatrics, University of Minnesota Medical School, and has as his hobbies painting and photography. Two of his photographs received honorable mention in contests of the Photographic Society of America International Exhibits sponsored by the Minneapolis and St. Paul Twin City Area Council of Camera Clubs.

Book Reviews

SKS IN THE PRACTICE OF MODERN OBSTET- CS—Silvio Aladjem, C. V. Mosby Company, 304 ges, $29.50.

Dr. Aladjem has enlisted a group of internationally :ated experts in the area of maternal and fetal medi- ie to contribute a series of topics chosen for this book stated in the preface "to represent areas that either are atively new to the practicing obstetrician or have seen ijor changes over the traditional concepts of obstetric re."

Chapters 1-6, 9 and 10 can be recommended as most levent to the practicing clinician. Chapters 1 through 3 Douglass, Brown and Freehafer, and Aladjem re- ectively, concern the detection and evaluation of pre- tal risks such as intrauterine growth retardation, RH oimmunization, intrauterine infections, toxemia, dia- :tes, assessment of gestational age. etc. These topics ould have benefitted had each author focused on one ea and approached this in greater depth; thus avoiding e repetition involved in the common theme of all three iapters.

Chapter 4 "Drugs and the intrauterine patient" by rs. Jaffe and Catz contains interesting information lating to benefits and hazards of various drugs admin- tered to the mother during the second and third tri- ester. Macintire discusses appropriate problems and nitations involved in prenatal genetic evaluation in hapter 5. The use of oxytocics to stimulate or induce bor are well described and reviewed by Dr. Cibils in hapter 6. A contemporary and useful description of ifertility evaluation and treatment is included by Dr. reenblat in Chapter 9. Complications encountered sing current techniques for pregnancy interruption are escribed by Dr. Manabe in Chapter 10.

In Chapter 8 Dr. Panigel, an experienced investigator, as briefly summarized and reviewed in vivo and in vitro xperimental models used to study placental permeability nd maternal fetal exchange in animals and the human. 'he final chapter by Ladimer discusses various medical- :gal problems and ramifications of numerous procedures nd evaluations related to perinatology.

Dr. Aladjem notes that the wide ranging background f the contributors offers to the reader "a point of view nbiased by common background or education." Such a election has the disadvantage of presenting diverse and ometimes controversial clinical approaches that may find ery little acceptance in the United States. For example: 1) The description in the first chapter by Dr. Douglass f specific electrocardiographic changes discriminating etween two types of intrauterine growth retardation, ne caused by a disturbed fetal pituitary adrenal axis 1 the fetus and the other true placental insufficiency, s too new and unsubstantiated to be of practical value o the practitioner. (2) Some of the nutritional hazards liscussed in the first chapter such as congenital beriberi lue to maternal thyamine deficiency and calcium defi- iency in the infant due to poor vitamin D intake in the mother are certainly problems largely concentrated in other sections of the globe. (3) A definite correlation is described in Chapter 3 between placental pathology presumably obtained via placental biopsy and changes in fetal chemistries, fetal hypoxia and distress during labor. This relationship is not universally accepted and of doubtful value at this time in the management of the obstetrical patient.

In addition to these areas of medical evaluation and management which perhap differ from country to country, there are several approaches suggested in this book which are simply out of date and, I hope, acceptable in no geographical area of modern medical practice. For example, on page 89 Dr. Jaffe suggests that 100 percent nitrous oxide administered with contractions is an acceptable method of achieving analgesia in labor. Most obstetricians would object to this and maintain that a much smaller quantity of nitrous oxide should be combined with at least twenty percent oxygen at any time in labor. Finally Dr. deWatteville in Chapter 7 appears to endorse the use of exogenous estrogen therapy in fairly large doses for threatened and habitual abortion, toxemia, and placental deficiency." This statement must reflect the fact that this chapter was prepared before evidence became available indicating the great danger inherent in estrogen therapy during pregnancy and its probable association with subsequent adenocarcinoma of the vagina in the female offspring.

Asa Elmore Seeds, M.D.
University of Minnesota

ANNUAL REVIEW OF ALLERGY, Claude Albee Frazier, Editor. 328 Pages, Medical Examination Publishing Company, Inc., Flushing, New York, 1972. Price $12.00.

Advances in allergy and immunology appear to be occurring with great rapidity today. Regardless of the journal, it is commonplace to find one or more articles concerning allergy or immunology. For this reason alone a monograph which attempts to gather together some of the more important and significant articles is welcomed. Of course this task is difficult and the judgment of any editorial board may be fallible.

The present volume is the first of this series and because of this, it reviews advances over the past several years. Presumably after this, one year only will be covered. The book is divided into twenty sections, each with its own editors. The sections themselves contain an introduction which helps orient the reader to the articles which are reviewed. For the most part the sections are well written.

Annual Review of Allergy certainly is a worthwhile volume for those physicians who must treat and manage the allergic patient. In addition because of the current emphasis on immunology, many other physicians will find this volume interesting and helpful.

Willard C. Peterson, M.D.
Minneapolis, Minnesota

The more physicians consider the hemodynamics o lowering blood pressure...

Most physicians now agree on the importance of reducing blood pressure in the hypertensive patient. But high blood pressure exists, of course, only as part of a complete clinical picture. The hemodynamic profile of well-established essential hypertension is characterized by elevated arterial blood pressure, normal cardiac output, and increased total peripheral resistance.

And so, physicians are increasingly concerned with the effects of an antihypertensive agent not only on blood pressure itself but also on the hemodynamic pattern—in short, with the total effect of the drug. *Does* it indeed help lower blood pressure effectively? *Is* peripheral resistance reduced? *Are* cardiac output and renal functions maintained? And, also, is there likely to be drug-induced postural hypotension serious enough to pose a threat to the patient's cerebrovascular status?

With this emphasis on overall drug performance has come a growing reliance on ALDOMET® (Methyldopa, MSD) in the treatment of sustained moderate hypertension.

With its unique hemodynamic profile, ALDOMET has drawn increasing attention and approval from physicians. First, of course, for its efficacy in

the more physicians rely on this unique antihypertensive

ering blood pressure. But
re are other considerations
vell. Cardiac output is usu-
maintained with no cardiac
celeration; in some patients
heart rate is actually
wed. Peripheral resistance
apparently reduced.
DOMET does not usually
npromise existing renal
ction; it generally does not
uce renal blood flow, glo-
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ually does not cause sympto-
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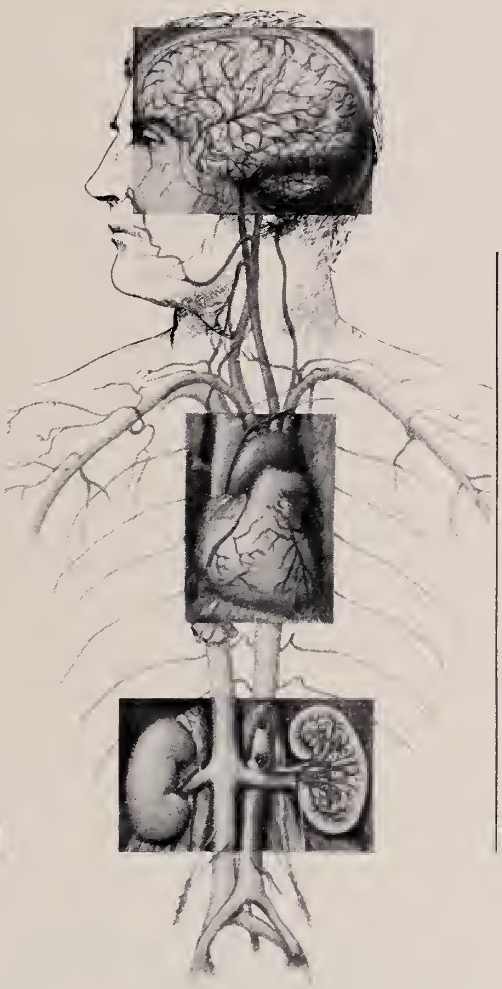

Some patients on continuous methyldopa therapy may develop a positive direct Coombs test. For more details, see the brief summary of prescribing information.

Contraindicated in active hepatic disease and known sensitivity to the drug. Not recommended in pheochromocytoma or pregnancy. It should be used with caution in patients with a history of liver disease or dysfunction. Discontinue the drug if fever, abnormal liver function, jaundice, or acquired hemolytic anemia occurs.

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For a brief summary of prescribing information, please see following page.

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(METHYLDOPA | MSD)

smoothly lowers blood pressure

Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis; known sensitivity. Not recommended in pheochromocytoma. Unsuitable in mild or labile hypertension responsive to mild sedation or thiazide therapy. Use cautiously in patients with history of previous liver disease or dysfunction.

Warnings: Acquired hemolytic anemia has occurred rarely in association with therapy with methyldopa. Should clinical symptoms indicate the possibility of anemia, hemoglobin and/or hematocrit determinations should be performed. If anemia is present, appropriate laboratory studies should be done to determine if hemolysis is present. Evidence of hemolytic anemia is an indication for discontinuation of the drug. Discontinuation of methyldopa alone or the initiation of adrenocortical steroids usually results in a prompt remission of the anemia. Rarely, however, fatalities have occurred.

Some patients on continued therapy with methyldopa develop a positive direct Coombs test; incidence reported has averaged between 10% and 20%. It rarely occurs in first six months of therapy, and if not seen within twelve months, is unlikely to develop with continued administration. Positive Coombs test is dose-related; lowest incidence occurs in patients on 1 g methyldopa or less per day. Reversal of the positive Coombs test occurs within weeks to months after discontinuation of methyldopa. Prior knowledge of a positive Coombs reaction aids in evaluation of cross match for transfusions. Patients with positive Coombs tests at time of cross match may exhibit incompatible minor cross match. When this occurs, an indirect Coombs test should be performed. If negative, transfusion with blood otherwise compatible in the major cross match may be carried out. If positive, advisability of transfusion with blood compatible in major cross match should be determined by hematologist or expert in transfusion problems.

Fever has occurred within first three weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first two to three months of therapy. Rare cases of fatal hepatic necrosis have been reported. Liver biopsy in several patients with liver dysfunction has shown microscopic focal necrosis compatible with drug hypersensitivity. Rarely, reversible reduction in leukocyte count with primary effect on granulocytes has been seen; reversible agranulocytosis has been reported. Methyldopa may interfere with measurement of creatinine by alkaline picrate method and of uric acid by phosphotungstate method. When used with other antihypertensive drugs, potentiation of antihypertensive action may occur.

Usage in Pregnancy and Childbearing Age—Not recommended in pregnancy. In women of childbearing age, weigh potential benefits against possible fetal hazards.

Precautions: Perform periodic hepatic function tests and white cell and differential blood counts during first six to twelve weeks of therapy or in unexplained fever. Discontinue if fever, abnormalities in liver function tests, or jaundice appears. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, spuriously high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. Discontinue drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Anesthetics requirements may be reduced; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension may occur after dialysis because methyldopa is removed by this procedure.

Dosage should be limited initially to 500 mg daily when following previous antihypertensive agents other than thiazides. Do not exceed recommended daily dose of 3.0 g. Patients with impaired renal function may respond to smaller doses than patients with normal kidney function. Syncope in older patients has been related to increased sensitivity in those with advanced arteriosclerotic vascular disease; this may be avoided by lower doses. Tolerance occasionally seen either early or late, but more likely between second and third month after initiation of therapy; increased dosage or combined therapy with a thiazide frequently restores effective control.

Adverse Reactions: Sedation, usually transient, may be seen during initial therapy or when dosage is increased. Headache, asthenia, or weakness may be noted as early, transient symptoms. Symptoms associated with effective lowering of blood pressure, including dizziness, lightheadedness, and symptoms of cerebrovascular insufficiency, are seen occasionally. Angina pectoris may be aggravated. Symptoms of orthostatic and exercise hypotension may occur; if symptoms occur, reduce dosage. Bradycardia, nasal stuffiness, mild dryness of mouth, and gastrointestinal symptoms including distension, constipation, flatus, and diarrhea occur occasionally; these can be relieved by reducing dosage. Nausea and vomiting have been reported in only a few patients. Sore tongue or "black tongue," pancreatitis, and inflammation of salivary glands may occur.

Weight gain and edema occur infrequently; if edema progresses or signs of pulmonary congestion appear, discontinue drug. Rarely, urine exposed to air may darken due to breakdown of methyldopa or its metabolites. Other rare reactions include breast enlargement, lactation, impotence, decreased libido, skin rash, mild arthralgia, myalgia, paresthesias, parkinsonism, psychic disturbances including nightmares, reversible mild psychoses or depression, reversible thrombocytopenia, drug-related fever and abnormal liver function studies with jaundice and hepatocellular damage (see **Warnings** and **Precautions**), rise in BUN, and a single case of bilateral Bell's palsy.

Supplied: Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., INC., West Point, Pa. 19486

ADDENDU

Let's make blood pressure "required reading" for all physicians.

With recent estimates that abo
23 million Americans have hig
blood pressure—and that half o
them are not even aware of it—
detection of the problem in
asymptomatic persons has become an issue of national importance.

Family physicians are being urged to take blood pressure readings as a matter of office routine, regardless of the presenting complaint or the reaso
for the visit. And because man
people do not see a family physician for relatively long periods of time, some experts are suggesting that ophthalmo
gists, gynecologists, dermatologists, orthopedists, psychiatrists, dentists, school nurses, family planning counselors, and other health-care personnel make blood pressur
reading a routine part of every examination or consultation.

Of course, a diagnosis of hypertension cannot be made on the basis of a single reading, but routine blood pressure reading
can uncover potential trouble i
a certain proportion of patients
And when trouble is suggested, further evaluation can be pursued more effectively.

Blood pressure-
"required readin
for all physician

Orthopedic Exhibits

A New Approach

MARTIN FINCH* and DAVID S. BRADFORD, M.D.†

THE DEVELOPMENT, transport and display of nedical data can consume a tremendous amount of time, money and energy on the part of the exhibitor as well as medical artist. A new method has been recently developed that has proven so highly effective and economical that we feel it justifies this report.

Method

The exhibit "Juvenile Kyphosis" is submitted as an example of how this new "Suitcase Exhibit" approach was used (Figure 1).

The first order of business was to organize and label the 25 Xrays to be used in the exhibit. These were labeled by a photographer using "Paratype" lettering (which could later be removed with film cleaner without damaging the Xray). Arrows, symbols, degree signs, patient initials, and dates were rubbed onto the Xray, using a plastic burnisher (Figure 2).

The labeled Xrays were mounted on a modified x-ray view box, and photographed with a 4 x 5 format view camera, using Tri X Pan film. The view box, which contained 17 15 W bulbs and a variable voltage transformer, allowed some areas of the Xrays to be intensified, while others were held back or dodged to bring out significant clinical details (Figure 3).

The 4 x 5 negatives of the Xrays were then cropped and masked by the artist. The desired final print enlargements were calculated and then indicated on the negative (Figure 4). At this point the artist prepared a comprehensive layout, on graph paper, for each of the seven exhibit panels using the measurements and calculated enlargements as a guide in designing the panels. From this comprehensive design on graph paper the artist began a "paste up" of the copy (wording) to be used and inking in boxes which would eventually contain the glossy x-ray prints (Figure 5).

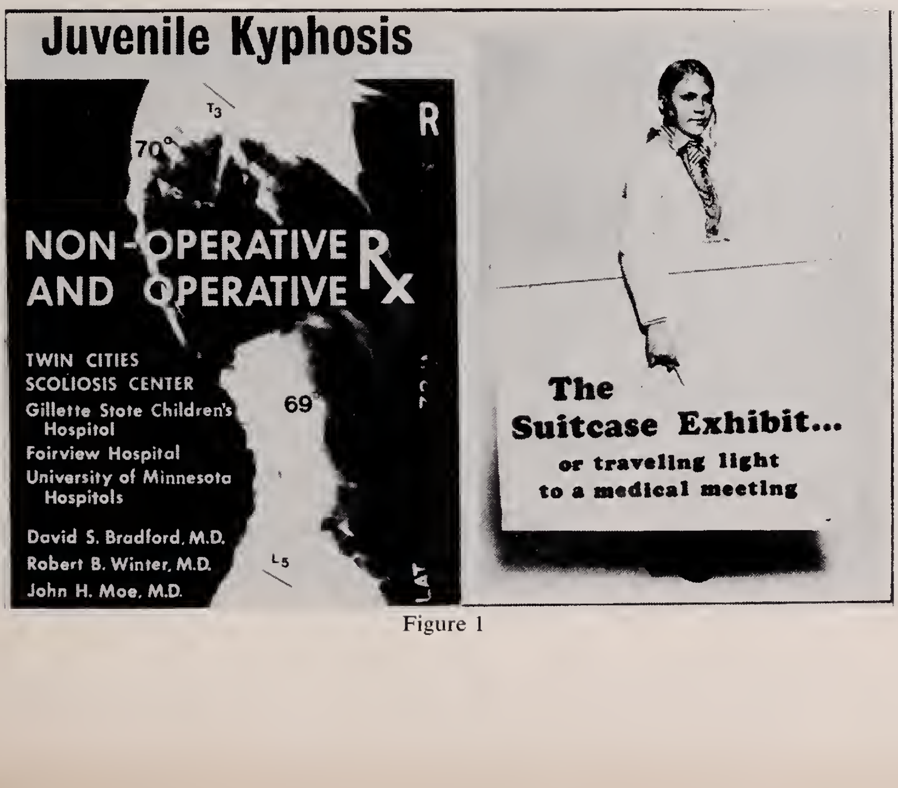
Juvenile Kyphosis
T3
70°
R
NON-OPERATIVE AND OPERATIVE Rx
TWIN CITIES SCOLIOSIS CENTER
Gillette State Children's Hospital
Fairview Hospital
University of Minnesota Hospitals
David S. Bradford, M.D.
Robert B. Winter, M.D.
John H. Moe, M.D.
69°
L5
LAT
The Suitcase Exhibit...
or traveling light to a medical meeting

Figure 1

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*Biomedical Graphic Communications Department, University of Minnesota Hospitals, Minneapolis, Minnesota

†Department of Orthopedic Surgery, University of Minnesota Hospitals, Minneapolis, Minnesota.

The final artwork for each of the seven panels was prepared on 11 x 14 illustration board, and sent out to a local photomural studio. The instructions were to photo enlarge and revêrse the artwork to a width of 40″ and length of 60″ (Figure 6). The murals were to be "dry mounted" on ¼″ styrofoam board. The cost for each panel was $37.00.

By the time that the photomural studio delivered the seven panels, all the glossy prints had been made to size and were ready for mounting onto the panels. Rubber cement was applied evenly to the back of each photograph, as well as to the surface of each panel. The cement was allowed to dry, and the prints were carefully mounted in each designated area (Figure 7). The photos were burnished with a soft rubber roller to assure good adhesion.

Figures 8 through 13 show six of the completed panels, and the seventh, or title panel, is pictured in Figure 1. In addition to the 25 Xrays, there were color prints of photomicrographs (Figure 8), surgical exposure (Figure 12) and patients (Figures 8 and 10). Black and white photos of patients were also used (Figures 11, 12 and 13).

After each panel was completed, it was hung up in our studio and photographed for departmental records and for later use in a brochure (Figure 14). For hanging purposes, gromets or shoe islets were punched in the upper right, upper middle, and left hand portions of each panel. These gromets support the weight of the panel securely and are wide enough to accommodate a headless nail, curtain hooks, safety pins, picture wire or any other device one might want to use to hang the exhibit up with.

Utilizing 8 x 10 glossy prints of each panel, we prepared a brochure to be handed out at the exhibit (Figure 16). We had 500 copies of this brochure printed, which contained an 8 x 10 reproduction of each of the seven panels for a cost of $160.00. We believe that every medical exhibit should have printed hand out materials, if only tabular information. When the viewer passes

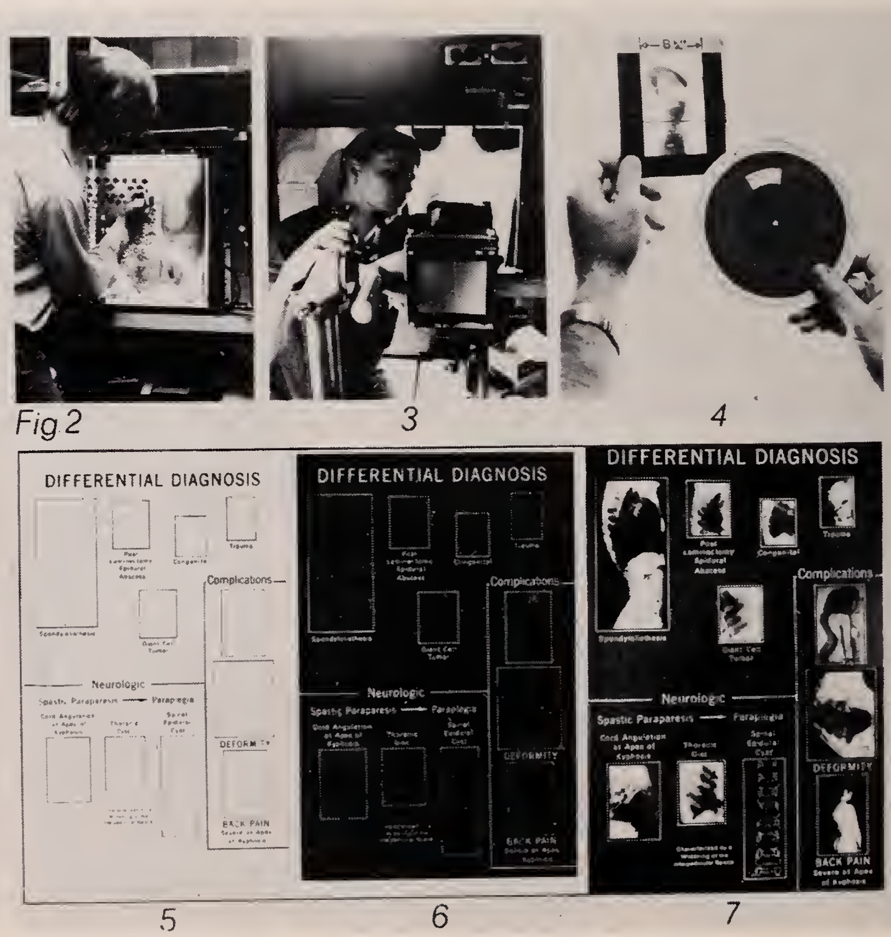
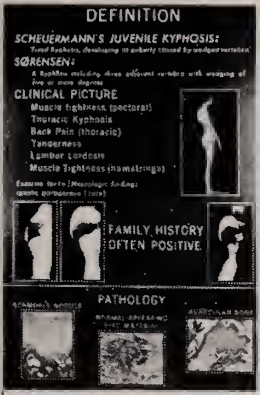


Fig 2 3 4

5 6 7

Figures 2, 3, 4, 5, 6 and 7



DEFINITION

SCHEUERMANN'S JUVENILE KYPHOSIS:

SØRENSEN:

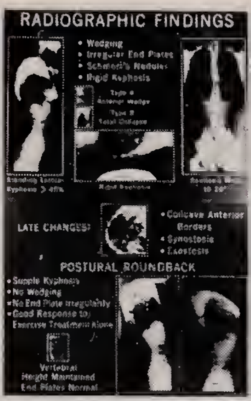
CLINICAL PICTURE

Muscle tightness (pectoral)
Thoracic Kyphosis
Back Pain (thoracic)
Tenderness
Lumbar Lordosis
Muscle Tightness (hamstrings)

FAMILY HISTORY OFTEN POSITIVE

PATHOLOGY

Fig. 8



RADIOGRAPHIC FINDINGS

- Wedging
- Irregular End Plates
- Schmorl's Nodules
- Rigid Kyphosis

Type A Anterior Wedge
Type B Total Collapse

LATE CHANGES:

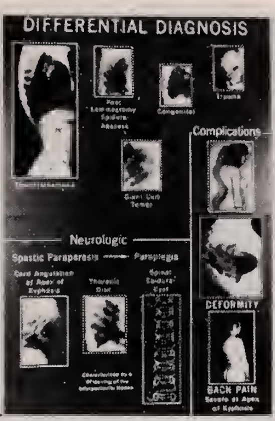
- Concave Anterior Borders
- Synostosis
- Exostosis

POSTURAL ROUNDBACK

- Supple Kyphosis
- No Wedging
- No End Plate Irregularity
- Good Response to Exercise Treatment Alone

Vertebral Height Maintained
End Plates Normal

9



DIFFERENTIAL DIAGNOSIS

Post Laminectomy
Congenital
Trauma
Giant Cell Tumor

Complications

Neurologic

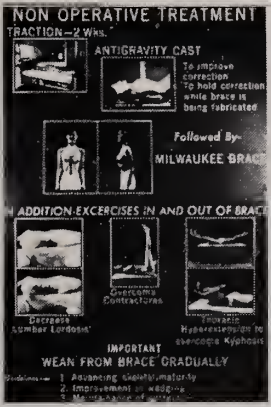
Spastic Paraparesis → Paraplegia

Cord Angulation at Apex of Kyphosis
Thoracic Disc
Spinal Epidural Cyst

DEFORMITY

BACK PAIN
Severe at Apex of Kyphosis

10



NON OPERATIVE TREATMENT

TRACTION—2 Wks.

ANTIGRAVITY CAST

To improve correction
To hold correction while brace is being fabricated

Followed By—
MILWAUKEE BRACE

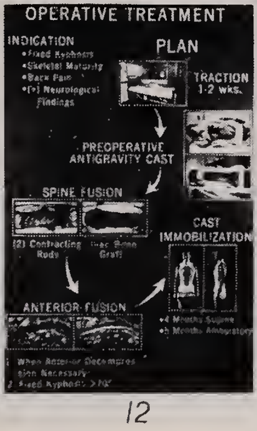
IN ADDITION-EXCERCISES IN AND OUT OF BRACE

Decrease Lumbar Lordosis
Overcome Contractures
Thoracic Hyperextension to overcome Kyphosis

IMPORTANT
WEAN FROM BRACE GRADUALLY

Guidelines— 1. Advancing skeletal maturity
2. Improvement in wedging
3. Maintenance of correction

11



OPERATIVE TREATMENT

INDICATION
- Fixed Kyphosis
- Skeletal Maturity
- Back Pain
- (+) Neurological Findings

PLAN

TRACTION 1-2 wks.

PREOPERATIVE ANTIGRAVITY CAST

SPINE FUSION

(2) Contracting Rods
Iliac Bone Graft

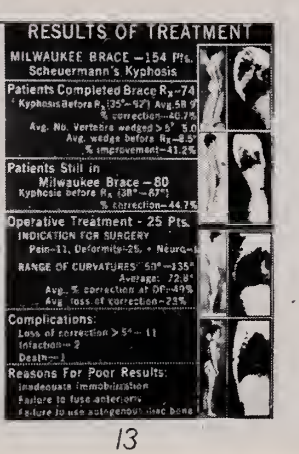
CAST IMMOBILIZATION

- 4 Months Supine
- 5 Months Ambulatory

ANTERIOR FUSION

1. When Anterior Decompression Necessary
2. Fixed Kyphosis > 70°

12



RESULTS OF TREATMENT

MILWAUKEE BRACE—154 Pts.
Scheuermann's Kyphosis

Patients Completed Brace R_x—74
Kyphosis Before R_x (35°—92°) Avg. 58.9°
% correction—40.7%
Avg. No. Vertebra wedged > 5° 5.0
Avg. wedge before R_x—8.5°
% improvement—41.2%

Patients Still in Milwaukee Brace—80
Kyphosis before R_x (38°—87°)
% correction—44.7%

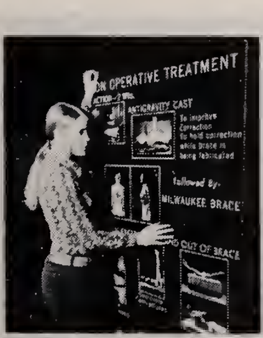
Operative Treatment - 25 Pts.
INDICATION FOR SURGERY
Pain—11, Deformity—25, + Neuro—1
RANGE OF CURVATURES 50°—135°
Average: 72.8°
Avg. % correction at OP—49%
Avg. loss of correction—23%

Complications:
Loss of correction > 5°—11
Infection—2
Death—1

Reasons For Poor Results:
Inadequate immobilization
Failure to fuse anteriorly
Failure to use autogenous iliac bone

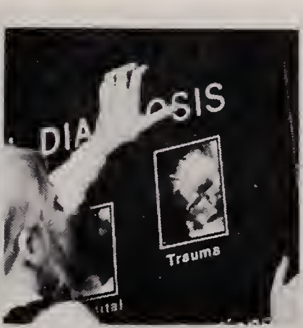
13

Figures 8, 9, 10, 11, 12 and 13



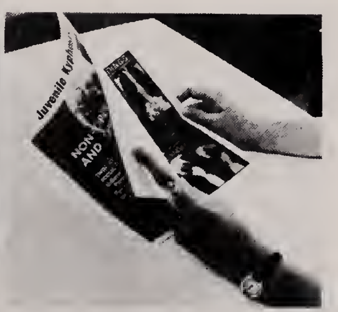
NON OPERATIVE TREATMENT
ANTIGRAVITY CAST
To improve correction
To hold correction while brace is being fabricated
Followed By-
MILWAUKEE BRACE
OUT OF BRACE

Fig. 14



DIA
OSIS
Trauma

15



Juvenile Kyphosis
NON
AND

16

IN ADDITION EXCERCISES IN AND OUT OF BRACE
Decrease Lumbar Lordosis
Overcome Contractures
IMPORTANT
WEAN FROM BRACE GRADUALLY
Guidelines—
1. Advancing skeletal maturity
2. Improvement in wedging
3. Maintenance of correction

17

ISES IN AND OUT OF BRACE

18

19

Figures 14, 15, 16, 17, 18 and 19

by the exhibit carrying a tote bag he will latch onto these. Weeks later, when he is back in his office leafing through his meeting notes he will come across the exhibit again in brochure form, thus you have gained added viewer time.

The exhibit is then ready for packing. Each panel is scored with a sharp knife across the middle of its face side and folded back (Figure 17), thus making it a 30″ x 40″ size from the previous 40″ x 60″. A customized carrying case is constructed of ¼″ styrofoam boards, the edges of which are joined and sealed with "Scotch Brand Filament Tape." The folded panels are carefully loaded into the carrying case to prevent chipping of the mounted photographs or scratching the photomurals (Figure 18).

The completed seven panel exhibit and carrying case weighed approximately 20 pounds, and afforded a 280″ linear panel display. As is usually the case it was finished at the last minute and rushed to the airport. We made special arrangements with the airlines, in advance, to have the exhibit put on and taken off the plane at the gate, rather than through the baggage terminal. This greatly reduced any possibility of damage or loss.

Discussion and Summary

The display of medical data is assuming an increasingly important role in surgical specialties. The cost of such displays can be staggering. We have found in the past that it is not infrequent for an exhibitor to spend over 3 to 4 thousand dollars in design, photography, and construction cost for displays. These displays often prove bulky and quite cumbersome to handle. Once the display has been constructed, one must also allow for rather significant transportation charges and labor expenses involved in moving the exhibit to a convention center, there having it dismantled and set up, subsequently dismantled at the conclusion of the meeting, and then retransported back to the point of origin. Therefore, the total cost, not to mention the inherent difficulties in assuring safety and punctual arrival of the exhibit, can prove overwhelming. The advantage of the present system lies in its low cost and convenience. The exhibit has proven quite light, weighing not more than 20 pounds and easily manageable. It can be carried under one's arm directly from the point of origin to the airplane, and then with the exhibitor to the destination. The exhibitor himself can put up the exhibit in a matter of five minutes, dismantle it and re-pack it in a similar amount of time and then carry it with him back to the point of origin. Labor costs are thus non-existent and the exhibitor is assured that his display arrives at the designated point on the necessary date.

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Idiopathic Systemic Fibrosis—Matas and Kremen (Page 280).

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Continuing Medical Education

On January 1, 1974, Minnesota became the seventh state to require evidence of continuing medical education as a basis for membership in its State Medical Association. Many more state medical associations are moving in this direction. A few states, by legislative action, have actually made continuing education a requirement for continuing licensure.

Discussion as to the advisability of this action and its impact on the quality of medical care was extensive within the Association's Committee on Medical Education. The Committee felt responsible for responding to increasing social and legislative pressures to establish some mechanism of assuring that the Minnesota State Medical Association members were keeping abreast of the rapid growth in medical knowledge. Alternatives were discussed and abandoned as being unfeasible. It was acknowledged that the continuing education plan is not a panacea but does provide a beginning toward association responsibility for the on-going education of its members. A list of those doctors who were members of the committee during the development of the plan follows. The Committee is one of the largest in our Association consisting of medical educators plus a broad representation of concerned physicians throughout the state.

Other states have found that this requirement increased the support of scientific meetings available in their areas and enabled the state associations to have some input into the content and quality of these programs through the mechanism of accreditation of programs. This was also the experience of the American Academy of Family Physicians which was the leader in this field.

The Committee first recommended to the House of Delegates in 1972 that evidence of continuing education be a basis for membership in the State Association. The 1973 House of Delegates approved the general plan and authorized the Council to inaugurate the plan. The Council, in the Fall of 1973, approved starting the requirement January 1, 1974. There only remains some minor changes in our Constitution and Bylaws which will provide the framework for enforcing the continuing education requirement. These changes will be submitted to the House of Delegates at their May meeting.

The requirements were modeled after the Oregon plan which has been in operation since 1970 and requires 150 credits per triennium. All specialty societies have responded accepting this as a minimum requirement, and many have offered specific ways in which their requirements can be fulfilled. These recommendations have been approved by the committee. The requirements are similar to those of the AMA's Physician Recognition Award and the American Academy of Family Physicians. Certification by either of these groups will be accepted as meeting the State requirement. The general requirements established by the Committee on Medical Education for those physicians whose specialty does not have specific requirements, are spelled out below. A manual including this information plus individual specialty society requirements will be printed and distributed to each member following the Association's Annual Meeting in May. Members will receive simple reporting forms annually. While compulsory reporting is not essential until the end of the first triennium (January, 1977) members are urged to keep current in their requirements and in their reporting.

With this step the Minnesota State Medical Association formally makes a commitment for quality medical care by its members. It is hoped that every member will cooperate in this program as we move into widening areas of medical responsibility.

H. P. Van Cleve, M.D.
Chairman
Committee on Medical Education

CONTINUING MEDICAL EDUCATION

1973 Medical Education Committee

H. P. Van Cleve, M.D., Austin
Arthur Aufderheide, M.D., Duluth
Eldon Berglund, M.D., Minneapolis
Paul F. Bowlin, M.D., Minneapolis
Henry Broker, M.D., St. Cloud
J. J. Buckley, M.D., Edina
H. Mead Cavert, M.D., Minneapolis
Thomas Comfort, M.D., St. Paul
David Craig, M.D., St. Paul
Edward Donatelle, M.D., Minneapolis
Herman Drill, M.D., Hopkins
W. R. Fifer, M.D., Minneapolis
Lyle French, M.D., Minneapolis
Roger Hartwich, M.D., Winona
Lyle Hay, M.D., Minneapolis
G. Benton Irons, M.D., Rochester
Herb Huffington, M.D., Waterville
Martin Janssen, M.D., St. Paul
Stephen Kieffer, M.D., Minneapolis
Kevin Lawler, M.D., St. Paul
Stanley Leonard, M.D., St. Paul
Fletcher Miller, M.D., St. Paul
P. J. Osmundson, M.D., Rochester
John Perry, M.D., St. Paul
Konald Prem, M.D., Minneapolis
Harley Racer, M.D., Minneapolis
Robert Reif, M.D., St. Paul
John J. Salchert, M.D., Minneapolis
James J. Tiede, M.D., Willmar
Francis Tiffany, M.D., St. Paul
John Welch, M.D., Rochester

General Requirements

150 credits per triennium required.

2 credits for each hour of attendance at local, state, regional and national specialty society scientific meetings in appropriate specialty.

2 credits for each hour in attendance at the MSMA Scientific Program.

2 credits for each hour of participation in specialty postgraduate courses sponsored by a medical school or other educational organizations generally recognized by appropriate specialty as qualified to conduct meaningful courses in that specialty.

2 credits for each hour of attendance at AMA Scientific Programs sponsored by or relating to appropriate specialty.

1 credit for each hour of attendance at hospital staff meetings and hospital scientific programs.

1 credit for each hour of participation in journal clubs, journal reading or audio digest. Limit, 60 credits per 3-year period.

1 credit for each hour of attendance at component society scientific programs.

1 credit for each hour of attendance at scientific programs of other generally recognized medical organizations not necessarily relating to specialty.

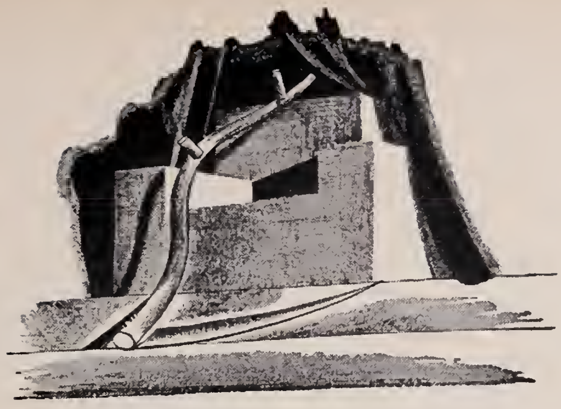
10 credits for preparing and publishing a scientific paper in a recognized professional journal, or for presenting such a paper to a medical or allied medical professional group.

2 credits for each hour of formal or informal teaching to medical or allied medical personnel. Limit, 90 credits per 3-year period.

1 credit for each hour of participation in area peer review panels.

Blue Earth Valley Medical Association Meeting

The Blue Earth Valley Medical Association will present "Recurrent Urinary Tract Infections/Update for the 70's" sponsored by Merrell-National Laboratories at their April 17th Meeting, 7:00 p.m., Fairmont Country Club.



In Memoriam

LLOYD H. RUTLEDGE, M.D.

Dr. Lloyd H. Rutledge, 82, Detroit Lakes physician, died January 2, as a result of carbon monoxide poisoning. A car located beneath the house had been left running in error. Mrs. Rutledge who was also in the house at the time was overcome with the poisoning.

He had practiced in Detroit Lakes for the past 50 years and just a year and a half ago had retired. Born in Freistatte, Missouri, Dr. Rutledge received his medical education at the University of Minnesota.

Dr. Rutledge was a Fellow of the American College of Surgeons, a member of the Minnesota Medical Foundation, American Association of Railroad Surgeons and was one of the first to report a case of tularaemia, "rabbit fever" in JAMA in 1927. He received recognition in 1964 for his achievements by being named in the "Who's Who in the Midwest." Dr. Rutledge was a member of the American Medical Association and the Clay-Becker County Medical Society and a Life and 50 Club member of the Minnesota State Medical Association.

He is survived by his wife, Nancy, and his sons, Dr. John Rutledge of Detroit Lakes, and Dr. Robert Rutledge of Fort Worth, Texas.

GEORGE WILLIAM CLIFFORD, M.D.

Dr. George Clifford, 66, Alexandria surgeon and founder of the Alexandria Clinic, died unexpectedly January 11, of a heart attack. He was a graduate of the University of Minnesota Medical School.

Dr. Clifford retired from the Alexandria Clinic five years ago, but he and his wife served on two voyages of the hospital ship, S.S. Hope, after his retirement. He was a member of the Minnesota State Medical Association, the American Medical Association, the International College of Surgeons, and the Park Region District and County Medical Society.

Dr. Clifford is survived by his wife, Elsa, and five children.

ROLLAND H. WILSON, M.D.

Dr. Rolland Harvey Wilson, 78, who retired from medical practice in Winona in 1965, died January 11. He came to Winona in 1929, was appointed Winona County Physician three years later and served in that capacity for 15 years. In 1950 he was elected city health officer.

Dr. Wilson was a member of the American Medical Association, the Winona County Medical Society and was a past president, 50 Club and Life Member and past president of the Minnesota State Medical Association.

He is survived by his wife, Hildred, and three sons, Dr. Louis Wilson of Rushford, David and Rolland.

JOHN A. DAHL, M.D.

Dr. John A. Dahl, 86, Minneapolis surgeon, died January 17 in Scottsdale, Arizona. He was educated at Loyola University Medical School and interned at St. Bernards Hospital in Chicago.

Dr. Dahl was a member of the American Medical Association and the Hennepin County Medical Society and a 50 Club and Life Member of the Minnesota Medical Association. He practiced medicine 60 years at the Deaconess Hospital in Minneapolis.

He is survived by his wife, Grace, daughter, Joyce.

EMIL J. FOGELBERG, M.D.

Dr. Emil J. Fogelberg, 73, Minneapolis surgeon, died December 13. He was a graduate of the University of Minnesota Medical School.

Dr. Fogelberg was a member of the American Medical Association and the Ramsey County Medical Society and a Life Member of the Minnesota State Medical Association. He was a past president of the Minnesota Academy of General Practice.

His wife, Ethelmae, survived him.

EDMUND G. OLMANSON, M.D.

Dr. Edmund G. Olmanson, 66, St. Peter physician, died December 17. His medical education was obtained at Northwestern University Medical School and he had practiced in St. Peter since 1936.

He was a member of the Nicollet-LeSueur County Medical Society and the American Medical Association and was an Associate Member of the Minnesota State Medical Association.

His wife, Donna; daughters, Joanne and Krist, and sons, Doctors M. D. Olmanson and Vern Olmanson of St. Peter survive him.

LUCIAN G. CULVER, M.D.

Dr. Lucian G. Culver, 74, St. Paul otolaryngologist, died February 20. He graduated from the University of Minnesota Medical School and interned at the Charles T. Miller Hospital in St. Paul.

In addition to being a member of the American Medical Association and the Ramsey County Medical Society, Dr. Culver was a Life Member of the Minnesota State Medical Association.

He is survived by his wife, Emily, son, Jeffrey, and daughter, Emily Ann.

RICHARD W. GIERE, M.D.

Dr. Richard W. Giere, 75, Minneapolis surgeon, died February 16. Born in Madison, Minnesota, Dr. Giere attended the University of Minnesota Medical School.

He was a member of the American Medical Association and the Hennepin County Medical Society and a Life Member of the Minnesota State Medical Association.

Dr. Giere is survived by his wife, Laura, son, Eric, and daughter, Priscilla.

ISABELL L. CAMERON, M.D.

Dr. Isabell L. Cameron, 79, Minneapolis gynecologist, died January 26. She was a graduate of the Boston University Medical School.

Dr. Cameron was a member of the American Medical Association and the Hennepin County Medical Society and a 50 Club and Associate Member of the Minnesota State Medical Association.

She is survived by her sister, Ione and brother, Uz.

W. RAY SHANNON, M.D.

Dr. W. Ray Shannon, 81, St. Paul pediatrician, died February 1. He was a University of Minnesota Medical School graduate.

Dr. Shannon was a member of the Ramsey County Medical Society and the American Medical Association and a 50 Club and Associate Member of the Minnesota State Medical Association.

He is survived by his daughter, Mary Jane, and sons, William R. Jr. and Robert J.

HUGO E. MILLER, M.D.

Dr. Hugo E. Miller, 69, Minneapolis urologist, died December 11. He was born in Colamer, Indiana, and attended the University of Minnesota Medical School.

Dr. Miller was a member of the American Medical Association and the Hennepin County Medical Association and a Life Member of the Minnesota State Medical Association.

He is survived by his wife, Kathryn, daughter, Susan, and son, H. Eugene, Jr.

HUBERT W. LEE, M.D.

Dr. Hubert W. Lee, 77, Staff member of St. Joseph's Hospital in Brainerd, died December 21. He was an eye, ear, nose and throat specialist, and a graduate of the University of Minnesota Medical School.

Dr. Lee was a member of the Upper Mississippi Medical Society and the American Medical Association and a Life Member of the Minnesota State Medical Association.

He is survived by his wife.

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Meeting

Twin City Urological Society

The Twin City Urological Society is sponsoring a Spring Urological Seminar similar to their program of last Spring, to be held *Saturday, April 20th, 1974* at the Marriott Inn in Bloomington, Minnesota.

The Seminar will start with morning pyelogram conferences. The afternoon session has scheduled as guest speaker, Dr. Ralph Straffon of the Cleveland Clinic. The scientific papers will be presented by Drs. Ahmad Orandi, David Utz, Hugh Williams, Elwin Fraley, Warren Brooker and Baxter Smith and will conclude with a panel discussion on, "The Management of Renal Mass Lesions," with Doctor Creevy as moderator.

Contact: Dr. A. S. Cass, St. Paul Ramsey Hospital, 222-4260.

Dr. Bernard C. Glueck, Director of Research at the Institute of Living in Hartford, Connecticut, will present a lecture at the University of Minnesota Health and Sciences Building—Unit A Room 2-620 (building is on corner of Washington Ave. and Union St. S.E. on the Minneapolis campus) at 8:00 p.m. Thursday, April 25th. The lecture title will be "Scientific Evaluation of Transcendental Meditation." There will be no admission charge.

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President's Letter

Thanksgiving

Word has come down from upper echelons that this, the last of my presidential scrivenings, is a place to scatter gratitude. Like Hamlet, I could exclaim, "Beggar that I am, I am even poor in thanks." Poverty of expression, however, should not be construed as ingratitude, for deep within is much sentiment, often disguised with a quip, sometimes with silence.

Many deserve thanks. First, my wife of over 30 years, whose ability to tolerate my nonsense has been amply demonstrated on many occasions, and whose fortitude in this year of many a lonely evening has been monumental. The product of that long-term romance, our seven children, also deserve thanks. These young people who, while they may not always agree with the middle class and somewhat conservative social and political views of their father, nonetheless have enough regard for the fourth commandment to view him with affection and even with respect.

The boundless energy and admirable cheerfulness of my partner demands mention. One problem in accepting medical society office is the enormous amount of time required—and all the while the office overhead goes on. One is concerned that only physicians from large groups or from the public sector will be able to accept these charges. Sacrifice from a small practice is real; the sacrifice from a solo practice is prohibitive. So, to Joe Gendron, my partner, who kept our active psychiatric practice going with great good will, I offer many thanks.

A share of gratitude must go to the paper industry of America. Its products came across my desk in an avalanche too massive to describe. Having only two eyes, I was unable to read it all. Indeed, at times I felt like the alcoholic who, despite his best efforts, is ultimately faced with the obvious ability of the distilleries to manufacture the stuff faster and in greater quantity than he can consume. Surely these paper mills are Vesuvius to our Pompei, burying us in an eruption that some future archeologist will excavate to find us lying with breath crushed from our lungs, a whole culture victim of its own productive exuberance.

Any medical society needs a staff. We in Minnesota are fortunate in the staff which serves us with loyal and dedicated zeal, with good will, and with good humor. To these, as well as to all past MSMA presidents for providing a model of dignified leadership, to the present officers, council members, and to all those who labor on various committees of our society, I offer a special note of gratitude. They are a good bunch who edify us by their example. To the staff of this journal for giving us an example of high grade journalism, to Elaine Nye, who is a professional in the best sense of that term, and to Reuben Berman, who sets a splendid model of a physician contributing to continuing medical education. My personal regret is that he is laying down this burden after three memorable years.

To all of you, gratitude for the letters you have sent in response to my column, some encouraging, some critical. They were all received in the happy knowledge that my efforts were read. Thanks also for the opportunity of serving as president of the MSMA. There is something about service to one's colleagues and about labor in the interests of our great profession that is stimulating and ennobling.

John J Regan

President
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JAMES H. DeWEERD, M.D.‡

When transplantation of a kidney is indicated, it should be done before too long a period of dialysis and a living related donor is preferred to a cadaver kidney. If no such donor is available, renal transplantation from a cadaver donor should not be denied the well-informed, intelligent, motivated patient who, after a trial of dialysis, prefers to take the risk. Enough high-risk patients survive with normal or nearly normal function to justify weighing all factors in each case individually and making the decision on an individual basis rather than a rigid policy. At the present time no well-informed patient who strongly desires transplantation is arbitrarily denied that option.

THE OVERALL NATIONAL success rate of renal transplantation has remained unchanged for the past several years.[1] The same has been generally true at the Mayo Clinic; but during this time there has been a steady increase in acceptance of high-risk patients, including a substantial number denied transplantation at other centers.

Since 1963, when the first Mayo Clinic renal transplant was performed, 173 patients have received 184 kidneys at this institution. Of these, 126 were from living related donors (LRD) and 58 from cadavers (CAD). Overall survival for the two groups is shown in Table 1. The longest-term survivor is presently well with a second transplant, nine years after his first allograft. Twenty-one patients are alive, well, and working, five years after renal transplantation.

Present Methods of Management

Our current method of immunosuppression was adopted in January of 1970. This method emphasizes the use of intravenous methylprednisolone (Solu-Medrol) in addition to azathioprine (Imuran). It has been fully described elsewhere.[2] Early success with this method led to our acceptance of more and more high-risk patients. The present report reflects this experience. From January 1970 through June 1973, 122 allografts have been performed with the overall survival rates shown in Table 1. The survival of patients for one and two years after transplantation is shown in Table 2. Survival of high-risk and of normal-risk patients is compared in Table 3. Only patients who have been shown to be at high risk on the basis of age, preformed antibodies (>10% of random cell population), or some serious extrarenal condition such as diabetes or myocardial infarction (see be-

TABLE 1
Overall Survival of Renal Allografts and Patients Through June 1973

Transplantations since	Donor type	No. pts	% surviving Allografts	% surviving Patients
November 1963	LRD	126	72	81
	CAD	58	53	71
January 1970	LRD	81	77	88
	CAD	41	60	71

TABLE 2
Survival of Renal Allografts and Patients by Postoperative Interval

Interval since transplantation	Donor type	No. pts	% surviving Allografts	% surviving Patients
2 yr or more	LRD	21	86	95
	CAD	14	50	64
1 yr or more	LRD	51	83	88
	CAD	22	46	59

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low) have been included.[3-5]

Comment

A comparison of the overall results from 1963 and those from 1970 indicates only moderate improvement. Both figures are influenced by the inclusion of more recent cases, in which the periods at risk obviously are shorter. Results in our previously reported earlier experience[6] (1963-1969) undoubtedly were influenced favorably by the exclusion of high-risk patients from transplantation.

An entirely different relationship appears when the results in normal-risk patients are compared with those at high risk. The difference is especially striking in the group of cadaver transplants, where graft survival was 80% in normal versus 49% in high-risk patients.

Aside from patients with preformed antibodies, who have a well-documented tendency to reject at a high rate,[5] there were a number of others at unusual risk. Illustrative of this type of patient are the following:

A 67-year-old man with diabetes mellitus, previous myocardial infarction, and chronic pulmonary emphysema; a heavy cigarette smoker for many years.

A 53-year-old man with a history of major bleeding diatheses, a myocardial infarct, gangrenous cholelithiasis, and two episodes of cardiac arrest during repetitive hemodialysis therapy.

A 15-year-old girl, the longest-term known survivor of a childhood syndrome known as pulmonary asphyxiant dystrophy.

A 63-year-old man with previous myocardial infarction.

A two-year-old infant cadaver recipient with metachromatic leukodystrophy.

A 27-year-old man with a history of portal hypertension, massive gastrointestinal bleeding, esophageal varices, and a prior splenorenal shunt.

A 39-year-old man totally bedridden with traumatic compression fractures of four vertebrae.

A 21-year-old man severely cushingoid after nine years of intermittent steroid therapy for renal disease and pancreatitis following bilateral nephrectomy.

A 58-year-old cadaver recipient with the additional hazard of anti N (cold-sensitive) antibodies requiring warming of the allograft prior to reestablishment of graft circulation, which increased the risk of acute tubular necrosis.

In addition, there were cadaver graft recipients over age 45, a group well-known to be at high risk.

The other group considered at high risk, despite generally good results in our experience,[7] comprises diabetic patients. This group totals 16, of whom two were more than 45 years old and also CAD allograft recipients. In one diabetic LRD recipient, iliac-vessel atherosclerosis was so advanced that blood flow adequate for good graft function never was established in two attempts at allografting.

The one-year and two-year survival rates may seem initially to be discrepant in that the two-year results are better. The explanation for this is inclusion in the one-year group (but not in the other) of 18 patients who received antilymphoblast globulin (ALG) in combination with large doses of methylprednisolone. Although the experience at the University of Minnesota with this preparation has been excellent,[4] the results in combination with our own use of methylprednisolone were unfavorable.

The use of ALG was abandoned after five deaths due to sepsis among the 18 recipients. The explanation for this unhappy result is probably twofold: (1) ALG was administered in doses of 15 mg/kg—half the dose employed by the University of Minnesota—in hopes of avoiding infectious complications; (2) the rate of rejection was not reduced, and the supplementation of ALG with concomitant large doses of methylprednisolone to reverse rejection resulted in unusual vulnerability to infection. We have had very few deaths from sepsis since discontinuing the use of ALG. Experience in the present year has again been favorable—a single death in 28 cases despite the continued inclusion of patients at high risk.

Complications have not been listed in detail because, with one exception, they differ little from those reported in two previous communications.[2,6]

TABLE 3
Survival of Renal Allografts and Patients at High and Normal Risk, January 1970 Through June 1973

Donor type	Risk category	Patients No.	Patients %	% surviving Allografts	% surviving Patients
LRD					
	High	31	38	65	77
	Normal	50	62	84	94
CAD					
	High	26	63	49	62
	Normal	15	37	80	87

The high incidence of thrombophlebitis and pulmonary embolism in our earlier experience has been reduced to zero since we began to give 5,000 units of heparin subcutaneously one hour prior to operation and at 12-hour intervals for five to seven days thereafter. We have continued to transplant kidneys to patients with a history of gastrointestinal bleeding and encountered no major difficulty from it.

The low incidence of significant side effects with intravenous methylprednisolone continues. Moderate to marked cushingoid facies occurs in approximately 6% of our allograft recipients. Aseptic necrosis of the hip has been proved in four of the 122 patients.

Only one urinary-tract fistula has been observed in our total transplant experience. The patient survives on dialysis after allograft nephrectomy.

With the exception of the experience with ALG and a brief series of cases in which prophylactic antibiotics were omitted on a trial basis, problems with wound sepsis have been minor, as previously described.[2]

Hyperacute or acute fulminant rejection continues to be an occasional problem despite careful typing and negative human leukocyte antigen crossmatching. It has occurred 8 times in 122 transplants. Reversal at best has been only temporary.

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It's The Law

Physician Liable for Delay in Transmitting X-ray Diagnosis

A 16-year-old boy was brought for emergency treatment to a hospital. The examining physician treated and sutured facial lacerations and ordered Xrays of neck and shoulders. On initial review of the Xrays the physician did not detect any injuries and concluded that the patient had a bruised and sprained neck.

The hospital radiologist reviewed the Xrays and mailed the report to the physician four days after the accident. This report indicated anterior compression of C5-6 vertebra.

Approximately two weeks after the accident, swelling developed in the patient's lower neck region. He was immediately hospitalized for extensive treatment including anterior fusion and posterior laminectomy, as well as removal of a herniated disc.

At trial, the jury ruled that the radiologist's failure to telephone the x-ray diagnosis to the family physician was one of the causes for subsequent complications. The court ruled in favor of the patient and against the radiologist in awarding damages for failure to transmit by telephone the important information learned from the Xrays.

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Merriman v. Toothaker, 515 p.2d 509 (Wash. Ct. of App., Oct. 19, 1973). The Citation 28:8, February 1, 1974.

Diabetic Nephropathy and Renal Transplantation

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Chronic hemodialysis and subsequent renal transplantation have been carried out in 17 patients with diabetic nephropathy. Thirteen (76%) are living from one to 38 months postoperatively. Seven (78%) of the nine patients who received a renal allograft 14 to 38 months ago are living and well with good to excellent rehabilitation.

WE SHALL USE *diabetic nephropathy* here to denote glomerulosclerosis, though more broadly it can refer to other chronic renal diseases seen in diabetic patients, such as pyelonephritis and necrotizing papillitis. The actual incidence and prevalence of glomerulosclerosis, pyelonephritis, mixed glomerulosclerosis-pyelonephritis, and necrotizing papillitis in the diabetic population are not known. The frequency of glomerulosclerosis in the diabetic population is dependent on age at onset of diabetes mellitus and its duration. Glomerulosclerosis is commonly seen in patients whose onset of diabetes occurs at 19 years of age or less and who have had their diabetes mellitus for 10 years or more.[1]

Pathologically, glomerulosclerosis may be of three varieties: nodular, diffuse, and exudative.[2,3] The exudative and diffuse lesions can be seen in other types of renal disease. Nodular glomerulosclerosis is considered to be pathognomonic of diabetes mellitus. The diffuse lesion is the most common type of glomerulosclerosis seen in diabetes mellitus. Accumulation of basement membranelike material in the mesangium of the glomerulus leads to development of the diffuse lesion, which may evolve into the acellular, eosinophilic PAS-positive nodule of nodular glomerulosclerosis.[2-5] The exudative lesion appears to be different from the diffuse and nodular lesions and it is characterized by a fibrin cap and capsular drop findings on microscopic examination. The exudative lesion is not specific to diabetes and may be seen in other forms of glomerulopathy.

Clinically, glomerulosclerosis may be present without any signs or symptoms of renal disease.[6] The first clinical evidence of diabetic nephropathy is usually the presence of persistent proteinuria which is followed over a period of five to 15 years by hypoalbuminemia, hyperlipidemia, peripheral edema, hypertension, and renal failure.[1,7] In the work-up of patients with chronic renal disease secondary to diabetes mellitus, caution should be exercised in performing intravenous pyelography if the serum creatinine concentration is high, for in diabetics the renal function may be further impaired after such a procedure.

Chronic pyelonephritis is common among diabetics, and in the end-stage of renal disease it may be indistinguishable clinically from diabetic glomerulosclerosis. Furthermore chronic pyelonephritis and glomerulosclerosis may be present together in diabetic patients with clinically evident renal disease. Necrotizing papillitis and coincidental chronic renal disease of other causes, such as glomerulonephritis and nephritis associated with lupus erythematosus, may also be present but are much rarer in diabetes mellitus. Consequently the diabetic patient with persistent proteinuria is highly suspect of having glomerulosclerosis. If there is evidence of diabetic retinopathy in the same patient, the probability of glomerulosclerosis is increased. If a diabetic patient less than 30 years of age has proteinuria and other clinical findings of chronic renal disease without evidence of retinopathy, renal biopsy is indicated to ascertain whether some other type of nephropathy is present that may be amenable to other forms of therapy.

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In the past the outlook for the patient with advanced renal failure due to diabetic nephropathy has been dismal.[1,7] Approximately 50% of juvenile-onset diabetics die from renal failure.[1,7] A smaller percentage of those developing diabetes after 30 years of age die of diabetic glomerulosclerosis. The proved benefit of chronic hemodialysis and renal transplantation as therapy for chronic renal disease provided the impetus for undertaking a similarly aggressive program in other high-risk diseases such as diabetes mellitus.[8] The patient with diabetes mellitus is at high risk because of the widespread implications of the disease—microangiopathy, macroangiopathy, and neuropathy.

Chronic hemodialysis (for 30 days or longer) and subsequent renal transplantation were carried out in 17 diabetic patients with nephropathy. There were 11 men and six women whose ages ranged from 24 to 67 years, averaging 38. Prior to dialysis or bilateral nephrectomy, their serum creatinine concentrations were 6 mg/dl or greater and their creatinine clearances 14 ml/min or less. Because chronic hemodialysis alone has produced discouraging results in diabetic nephropathy,[9] it was utilized only during the interval between bilateral nephrectomy and subsequent renal transplantation in these 17 patients.

The criteria for the selection of the diabetic recipient and the donor for renal transplantation are shown in the Table.

TABLE
Criteria for Selection of Diabetic Recipients of Renal Transplants and of Donors to Them

- For selection of the diabetic recipient
  - Age: less than 50 years
  - Intelligent cooperation and rehabilitation potential
  - Absence of other chronic diabetic complications (retinopathy; cardiovascular disease, cerebrovascular disease, peripheral vascular disease)
  - Normal bladder function
- For selection of the donor
  - Good general health
  - Good renal function
  - Good match on histocompatibility studies
  - No evidence of diabetes mellitus (normal results on oral glucose tolerance test and oral cortisone glucose tolerance test)

The risks to the donor are minimal, including the risk of anesthesia and the remotely possible increased risk of diabetic nephropathy in the patient with one kidney.

Although these criteria have been adhered to for the most part, two patients more than 50 years of age have received renal allografts, as have other patients with other chronic diabetic complications (retinopathy, coronary-artery disease, and peripheral vascular disease).

Major problems encountered in the management of the diabetic patient on chronic hemodialysis include:

1. Aggravation of the diabetic retinopathy with retinitis proliferans, neovascularization, vitreous hemorrhages, and blindness.
2. Aggravation of diabetic neuropathy with increasing weakness and pain in the extremities.
3. Hyperosmolar syndrome with increased thirst and lethargy but usually no coma.
4. Difficulties in monitoring diabetic control without adequate urine specimens particularly when the patient has been nephrectomized in preparation for renal transplantation.
5. Congestive circulatory failure with dyspnea, peripheral edema, and weight gain.

No specific therapy has been devised for prob-

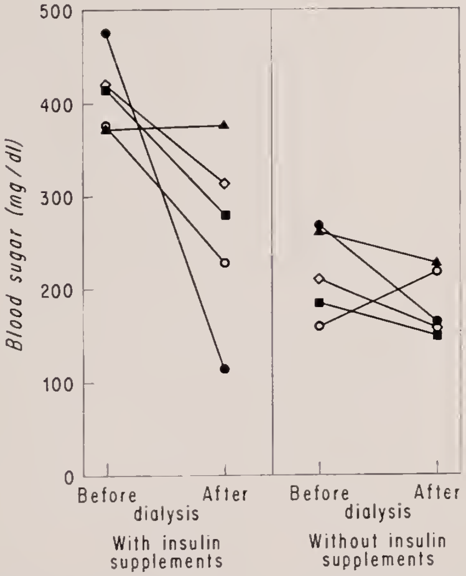

Fig. 1—Mean blood glucose values determined in five patients before and after dialysis, with and without insulin.

lems 1 and 2 above, other than a shortening of the period of dialysis by transplantation as soon as feasible.

For problems 3 and 4, blood glucose is measured before and after hemodialysis to gauge insulin needs. Crystalline zinc insulin is given during dialysis to supplement the usual daily insulin program in an attempt to keep the post-dialysis blood glucose less than 300 mg/dl. Ten units of crystalline zinc insulin are given for every 100 mg of the predialysis blood glucose above 300 mg/dl.

The means of multiple blood glucose values determined before and after dialysis with and without supplemental administration of insulin are shown in Figure 1. There is a significant difference in the means before and after hemodialysis when supplements of insulin are given ($P < 0.05$), but not when the supplements are withheld. The response of the same patients during dialysis did not differ significantly when supplemental insulin was given or not given during dialysis. No significant correlation could be found between the changes in blood glucose and the total insulin dosage given, whether insulin supplements were provided or not. The dialysis bath maintains a glucose level of 200 mg/dl, and thus may provide a satisfactory safeguard against hyperglycemia as well as against inadvertent hypoglycemia during dialysis. So supplemental insulin therapy appears to be relatively safe during hemodialysis. Such supplemental insulin treatment may promote and maintain glycogen deposition in both the liver and muscle and reduce gluconeogenesis. Additional supplements, therefore, should be given whenever feasible during hemodialysis.

Problem 5, congestive circulatory failure, may be related to the greater prevalence of ischemic heart disease among diabetics and to their intakes of salt and water. They may be loath to restrict salt intake along with carbohydrate intake and may be habituated to drinking large quantities of water. Serum sodium concentration and serum osmolality are usually in the normal range, suggesting that both salt and water are ingested in excess. Instead of the usual gain of approximately 1.5 to 3 kg between dialyses, some diabetic individuals gain 3.5 to 7 kg in that interim. If hyperglycemia and its hyperosmolality can be controlled with adequate insulin therapy, restriction of fluid and salt may be effective in reducing circulatory overload and perhaps correct the inappropriate thirst these patients feel despite fluid overload and satisfactory diabetic control. Whether congestive heart failure during the period of hemodialysis therapy is more common in diabetic patients than in other patients with chronic renal disease is a moot point.

In the post-transplantation period, three major problems compound the management of the diabetes mellitus. First, the discrepancy between the values from simultaneous (within 30 to 60 minutes) tests for glucose in blood and urine is more pronounced after renal transplantation. Although there is a significant correlation between results of the blood tests and those of semiquantitative urine tests, for all patients ($P < 0.01$), there still

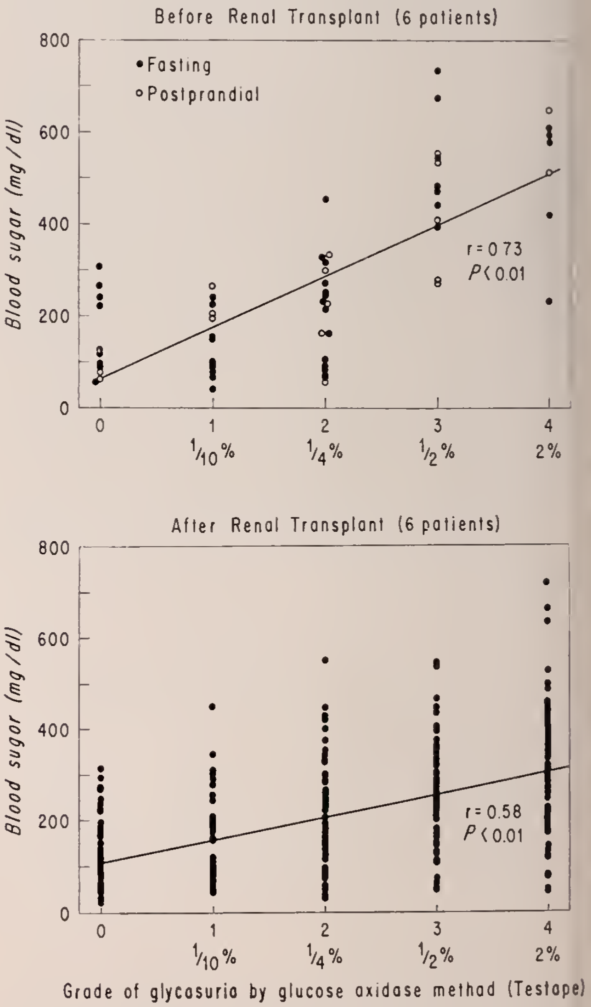

Fig. 2—Results of simultaneous blood and semi-quantitative urinary glucose tests made before and after renal transplantation in six patients.

are instances in which urinary glucose values do not correspond satisfactorily to the blood glucose levels (Figure 2); and this may lead to difficulty in diabetic management if the urinary tests are relied upon exclusively. The blood glucose values and those from the semiquantitative urinary glucose test correlated less well after renal transplantation than before, and that difference was significant ($P < 0.01$.)

Second, 40 to 1,000 mg of methylprednisolone is administered intravenously on an intermittent basis to prevent allograft rejection. All patients are taking maintenance doses of prednisone and azathioprine orally when dismissed from the hospital three weeks after transplantation. Use and withholding of methylprednisolone make no significant difference in the correlation of blood and urinary glucose values. The correlation is stronger when supplemental insulin is given ($P < 0.05$) on the day the methylprednisolone is administered intravenously.

Third, the insulin requirement is higher after renal transplantation. This rise is attributable to the steroid administration and to functioning of the kidney, which participates in the degradation of insulin.[10]

In response to these three major problems of diabetic management in the post-transplantation period, fasting and postprandial blood glucose concentrations are measured three or four times daily to gauge insulin requirements, particularly in the first three postoperative months. After three to six months the diabetes appears to stabilize—partly because further intravenous administration of methylprednisolone is not usually necessary. At this point the urinary glucose tests can be used as a rough guide for insulin adjustment. However, the method of monitoring diabetic control has to be individualized, for some patients continue to have glycosuria despite satisfactory blood glucose concentrations (less than 150 mg/dl). Conversely aglycosuria may occur with unsatisfactory blood glucose concentrations (200 mg/dl or more), but this is far less common.

An unusual finding in one of our patients who underwent renal transplantation was superficial

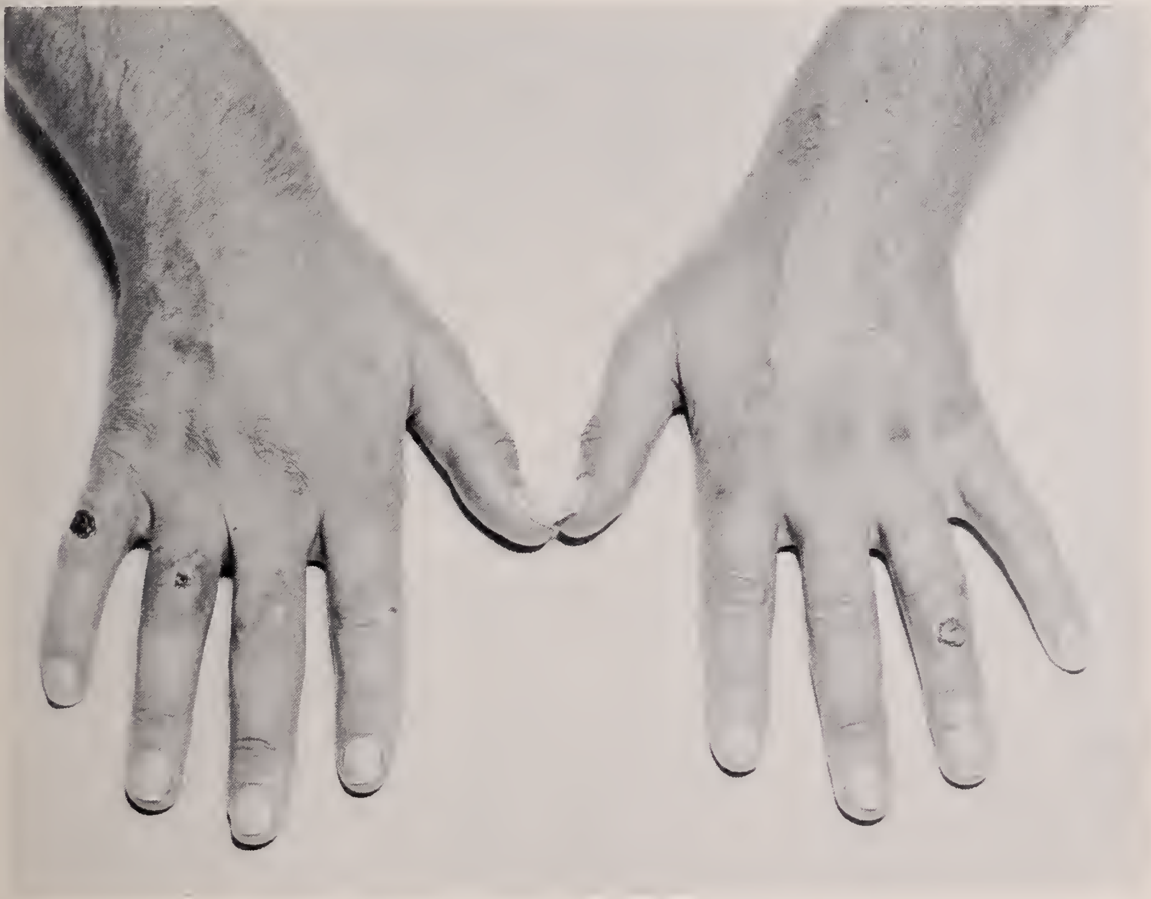

Fig. 3—Unusual post-transplantation necrotic lesions of fingers.

necrotic, gangrenous lesions in the fingers (Figure 3). These lesions did not appear to be related to the arteriovenous fistula created previously for hemodialysis. They were bilateral and slow to heal. Another patient had gangrene of the toes, which is a more common finding in diabetics and required a below-knee amputation. This patient is doing well with a prosthesis for walking.

Infection and sepsis are no more troublesome in diabetic patients than in others who have received renal allografts. Lymphosarcoma, pancreatitis, and hyperparathyroidism have not been seen as yet in our diabetic group.

The other chronic diabetic complications tend to improve after renal transplantation. The retinopathy has remained quiescent in all of our cases and visual acuity has improved subjectively. The neuropathy also has improved in all patients. There is no apparent effect to date on the cardiovascular disease.

Despite all the factors cited the survival of these diabetic patients who have undergone renal transplantation has been encouraging. Of the 17 patients four have died: one from bacterial pneumonia, another from a postoperative pulmonary embolus, another from allograft rejection two months after transplantation, another from wound and generalized sepsis. Five of the 17 patients received cadaveric allografts; the rest had living related donors. Of these latter 12, nine are doing well with satisfactory renal function (serum creatinine 1.9 mg/dl or less) ranging from one to 38 months after the transplantation. An additional patient has survived rejection of two renal allografts from living, related donors, and is currently on hemodialysis. The remaining two patients have died.

Of the five patients who had received a cadaveric allograft, three are living with satisfactory renal function three to 15 months after the transplantation.

Seven of the nine patients who received a renal allograft 14 to 38 months ago are living and well with complete or nearly complete rehabilitation.

Summary

Chronic hemodialysis is more appropriate for those patients awaiting renal transplantation than as the sole mode of therapy for an unlimited period. Aggravation of the diabetic retinopathy, and neuropathy, hyperosmolar syndrome, difficulties with diabetic management, and congestive circulatory failure may occur during the period of chronic hemodialysis.

In the post-transplantation period, difficulties with interpreting results of semiquantitative tests of urinary glucose, intermittent large intravenous doses of methylprednisolone, and rising insulin requirements complicate the management of the diabetes mellitus.

Frequent determinations of blood glucose are necessary to gauge insulin needs, both in the chronic hemodialysis period and in the early post-transplantation period.

Retinopathy and neuropathy may improve in the post-transplantation period.

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St. Joseph's Hospital, Brainerd

Officers for 1974 elected at a medical staff meeting at St. Joseph's Hospital were: Dr. Douglas L. Johnson, Brainerd ophthalmologist, chief of staff; Dr. Forrest B. Spieler of Pequot Lakes, vice chief of staff; Dr. Mark A. Muesing, Brainerd, treasurer and Dr. Gary G. Kohls, Pine River Clinic, secretary.

Lower-Urinary-Tract Infection

Recent Developments

JOSEPH W. SEGURA, M.D.* and LYNWOOD H. SMITH, M.D.†

In treating "infections" of the lower urinary tract, it is important to determine whether or not an infection does, in fact, exist, and if so, to confirm the offending organism. In the growing problem of nonspecific urethritis, Chlamydia organisms should be considered a possible cause.

THE SIGNIFICANCE OF lower-urinary-tract infection varies from youth to old age, from male to female, and from patient to patient. Its importance in children as an indication of anatomic abnormalities is well-recognized, but the most perplexing aspect remains the diagnosis and treatment of recurrent urinary-tract infection in women. Recent work has a number of therapeutic implications; but treatment is dependent on diagnosis, and it is still true that the central issue in the management of lower-urinary-tract infection is whether an infection does, in fact, exist.

Diagnosis

In most cases a properly collected midstream urine specimen will be satisfactory for microbiologic purposes, and a specimen of great diagnostic reliability may be obtained by methods described previously.[1] It should be emphasized that specimens produced at home and brought to the laboratory are totally useless for the demonstration of urinary-tract infection.

Although nothing else is equal to urine inoculated in appropriate media and cultured in the microbiologic laboratory as a basis for determining the presence or absence of infection, a number of simple, inexpensive systems are available which enable the physician to perform reliable urine cultures on a practical basis in the office. Further, ordinary Gram staining of uncentrifuged urine, if positive, will correlate with significant bacteriuria in a large percentage of cases.[1] Whatever culture methods are used, inoculation should be done as soon as possible unless the specimen is refrigerated. A major source of error is delay between collection and inoculation, a problem that often is due to transportation difficulties. During 30 minutes of unrefrigerated waiting time, insignificant colonies will multiply to significant size and larger. The presence of pyuria is a most inconsistent indicator of infection. Indeed, 50% of patients who have bacteriuria have no pyuria whatsoever.

The most intriguing development of the past few years is Stamey's[2] demonstration that the introital region of women who have never had a urinary-tract infection was devoid of pathogenic gram-negative bacteria, whereas pathogens were recoverable from the introitus of patients who had histories of infection. King and Leadbetter[3] have demonstrated the same correlation of the vaginal flora among pediatric patients. Further, these bacteria that caused urinary-tract infections could be found on the introitus prior to their appearance in the urine. What factors may be responsible for this difference have not been elucidated, although vaginal pH may be one of them. If so, it should be possible to predict what bacteria will be responsible for the next urinary-tract infection, and it may be possible to prevent such infection by affecting the flora of the introital area. This reasoning forms the basis for long-term treatment of women with frequent, recurrent urinary-tract infections in whom thorough urologic evaluation has ruled out the possibility of anatomic abnormalities or foci of infection in the urinary tract. We usually reserve this long-term treatment for those who have more than three or four urinary-tract infections per year.

Treatment

The choice of a suppressant involves several factors, among which are effectiveness, ease of administration, economy, and toxicity. Also, the suppressant should not affect the composition of bowel flora—for if, as seems most likely, introital pathogens originate in feces, then this restriction lessens the likelihood of generating resistant organisms to re-colonize the introitus.

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See editorial, page 391.

Nitrofurantoin, in a dosage of 50 mg twice daily, fulfills many of these criteria. It is relatively nontoxic (though it cannot be used in patients with chronic renal failure or creatinine clearance <60 ml/min); it does not affect the composition of bowel flora; the twice-daily schedule is easy for patients to manage; and it is not particularly expensive.

Methenamine, 0.5 to 1.0 g four times daily, is an excellent suppressant entirely suitable for long-term therapy. It has low toxicity, is cheap, and has no effect on fecal organisms. The urinary pH must be maintained at pH 6.0 or less to hydrolize methenamine to formaldehyde, the active agent. Otherwise methenamine is completely ineffective. For practical purposes it is necessary to acidify the urine with 500 mg of either ammonium chloride or ascorbic acid four times daily. Ammonium chloride is usually more effective in this regard. The urinary pH must be measured every day with a strip of nitrazine paper. Inability to acidify the urine may occur for several reasons, but frequently indicates the presence of a urea-splitting organism. Disadvantages of this program include the necessity to take rather many pills per day and the fact that daily checking of pH is beyond some patients.

Oral penicillins also can be used as suppressants; and they have effect against certain gram-negative pathogens, including *Proteus mirabilis*.[2] Further, penicillin can be given to patients with poor renal function. Except for allergies, the drug is practically nontoxic. However, the gram-negative effectiveness of penicillin is limited, and penicillin does affect the bowel flora.

Sulfas are a poor choice for suppressive purposes. They affect fecal and introital flora rapidly, and resistant organisms appear soon.

With whatever agents, the suppressant program is continued for six months. A detailed discussion with the patient regarding the rationale behind this therapy will pay dividends in compliance with the program.

At the end of the six months the medication is stopped and a period without therapy is tried. The program outlined is frequently successful, but evaluation is not possible unless reliable specimens are obtained for determining whether the infection is persisting. The ubiquitous urethral syndrome (frequency, dysuria, suprapubic pain) may supervene in anyone, and its presence does not mean that the treatment has failed. In some cases where infection during suppressive therapy has been proved, the program has been augmented with nitrofurazone vaginal suppositories twice daily. This is of uncertain benefit but may be worth trying in the circumstances. Treatment for recurrent urinary-tract infection in women will never be easy; however, the program described has been very helpful in properly selected cases.

Special Problems

Nonspecific urethritis (NSU) is a recalcitrant problem of ever greater importance in an era of increasing sexual permissiveness. NSU frequently occurs in persons treated for gonorrhea with agents such as penicillin or ampicillin, as well as other antibiotics. Recently *Chlamydia* organisms have been cultured from such patients with surprising regularity. These are neither viruses nor bacteria: they contain both DNA and RNA, and both cell and enzyme systems. Consequently they are inhibited to a greater or lesser extent by various antibiotics. Dunlop et al.[4] recovered *Chlamydia* organisms from 45% of men with NSU and from one-third of the women who were sexual partners of these men. Richmond et al.[5] were able to culture *Chlamydia* organisms from 39% of men with non-gonococcal urethritis and from 32% of men with gonorrhea; but only five of 92 control patients (5%) had such organisms in the urethra. Just how *Chlamydia* organisms are related to NSU and how that is related to gonorrhea remain to be determined. Such infection may be venereally transmitted and cause urethritis by itself, or it may be activated only by previous infection such as gonorrhea. Exact determination of these matters may provide the answer to the frustrating problem of treatment for NSU. Investigations in this direction are underway currently in this institution.

The treatment for *chronic prostatitis* has never been satisfactory. One of the major reasons for this is the fact that it has long served as a wastebasket diagnosis. Perineal pain and low backache, associated with periodic episodes of dysuria, may suggest the diagnosis; but demonstration of a pathogenic bacteria in the prostatic secretion is a sine qua non. Yet even when the physician is reasonably sure chronic prostatitis exists, therapy is often unsatisfactory because of the fact that most antibiotics will not attain therapeutic concentrations in prostatic fluid. Stamey[2] demonstrated that only the basic macrolides (erythromycin and triacetyloleandomycin) could be recovered in therapeutic concentration in prostatic fluid. Unfortunately, the effectiveness of these drugs does not encompass the gram-negative pathogens most commonly found in cases of true chronic prostatitis. The possibility that the combination drug cotrimoxazole (trimethoprim-sulfamethoxazole) may be effective in chronic prostatitis has raised the hope that effective treatment for this entity may at last be at hand. Studies by Meares[6] and Chesley and Dow[7] have indicated that this medicament can produce various degrees of success in many patients with true chronic prostatitis. At this time, however, use of this drug for chronic prostatitis is still investigational in the United States. If further clinical experience confirms its effectiveness in chronic prostatitis, and if the drug is cleared by the Food and Drug Administration for this indication, then this will clearly be the drug of choice in the treatment for chronic prostatitis.

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Cover Photo

"Miners' Canyon"

Dr. George M. Klc-Mikusciak, family physician at the Western Martin Medical Clinic in Trimont, Minnesota, took the cover photo in the Fall of 1972 near Chisholm. Dr. Kelcey (as English-speaking people call him) used a KONICA Autoreflex T camera using 135 mm Hexanon lens and KODACHROME II film. The world-unique and magnificent "Man-made" hills and the valley have been known as "Miners' Canyon" in memory of thousands of workers, mostly immigrants from south-eastern European countries who picked up—manually—an immense amount of Taconite (an iron-richest ore) from the Pillsbury Mine, which was located there in the Iron Range of the north-eastern corner of Minnesota.

A native of Slovakia, George M. Klc-Mikusciak, received his M.D. and almost simultaneously his M.Sc. (Chemistry-Biochemistry) from Charles IV University, Prague in 1959. He holds an appointment as Assistant-Professor at Slovak Postgraduate School of Medicine, Bratislava, Czecho-Slovakia. After a successful escape from his Communists' dominated country in 1966 and on completion of all professional requirements he became a licentiate of the Medical Council of Canada in 1970. At the same time he passed Federal Licensing Examination in the United States and received his license to practice medicine in Illinois and Minnesota.

The Pillsbury Mine, part of the Monroe group of mines viewed in this picture was named for John S. Pillsbury, Governor of Minnesota and owner of the property when iron ore was discovered in 1893 by Edmond J. Longyear. Mining operations were begun here in 1898 by the Lake Superior Consolidated Iron Mines and were continued in 1901 by the Oliver Iron Mining Division of the U.S. Steel Corporation until the mine was exhausted in 1961. This mine is one of many which together make up the world famous MESABI (Chippewa Indian for "Giant") IRON RANGE. The Monroe group of mines has to date produced 108,081,485 of the Mesabi's 2,370,676,060 tons of iron ore that helped build our country's industrial might and sustain through two World Wars.

Treatment of Chronic Renal Failure

CARL F. ANDERSON, M.D.*

Successful management of a patient in renal failure depends on a thorough evaluation to determine his ideal sodium and protein intake. Since both values are variable, satisfactory adjustments require vigilance by both patient and physician.

Renal failure is present when the blood levels of waste products that depend on the kidneys for excretion are increased. In actual practice, use of the term renal failure implies an increase in blood urea and serum creatinine values. In most adults, a serum creatinine concentration over 2.5 mg/dl requires treatment to minimize the effects of nephron loss.

When I see a patient in renal failure, I try to determine its cause, look for any reversible features, and—if the failure is chronic—begin specific treatment.

Investigation

History

1. Is there a family history of renal disease? (Polycystic renal disease, Alport's syndrome, and renal lithiasis are the three familial renal diseases I encounter most often in cases of chronic renal failure.)
2. Has any prior urinalysis been abnormal? Has the patient ever noted gross hematuria?
3. Has the patient passed stones or gravel per urethram? Has he had gout?
4. Has he had hypertension?
5. Has the patient experienced dysuria or severe costovertebral pain and fever?
6. Does the patient have a disturbed pattern of urination (nocturia, incontinence, or a sense that bladder emptying is incomplete)?
7. What medicaments is the patient taking currently?
8. Does the patient have symptoms that suggest uremia (anorexia, nausea, vomiting, fatigability, pruritus)?
9. How much sodium does the patient ingest daily? (Estimation of sodium intake is important because the total body sodium determines the extracellular fluid volume and greatly influences the blood pressure in patients with chronic renal failure.)

Physical Examination

The physical findings in chronic renal failure, which depend on extracellular fluid volume (ECFV) may be considered together. The ECFV is comprised of the plasma volume and the interstitial fluid volume. In a normal adult, plasma volume equals 5% of the body weight (for instance, 5% of 70 kg body weight would be 3.5 liters of plasma). The interstitial fluid equals 15% of the body weight (15% of 70 kg would be 10.5 liters of interstitial fluid).

In a patient with chronic renal failure, expansion of the ECFV is usually accompanied by hypertension, elevation of jugular-vein pressure, and peripheral edema. Further expansion may lead to pulmonary congestion and frank heart failure with an audible ventricular gallop (S_3). Depletion of ECFV is associated with orthostatic hypotension (systolic blood pressure falls more than 10 mm Hg when the patient stands), low jugular-vein pressure, and often a history of weight loss.

Other physical signs include: (1) enlargement of kidneys (ascertained by palpation); (2) enlargement of bladder (ascertained by palpation); (3) rectal sphincter tone and, in men, increased prostate size; (4) distal brown arcs in fingernails[1,2] (Figure)—which occur frequently in chronic renal failure; and (5) distal peripheral neuropathy—usually more demonstrable in lower extremities. There may be paresthesia, diminution and then loss of vibratory sense in the feet,

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See editorial, page 392.

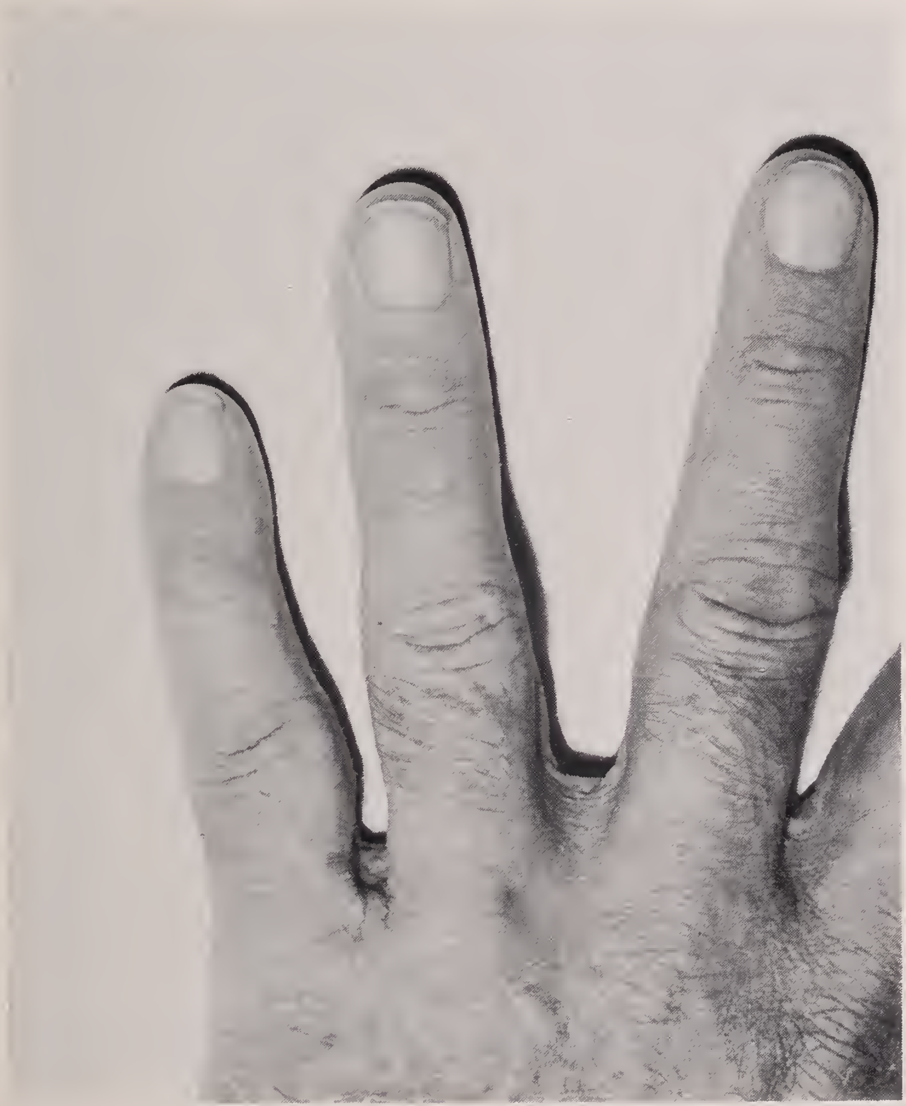
followed by loss of ankle jerks.

Laboratory Examination

Minimal laboratory studies in these cases include: (1) complete blood count; (2) urinalysis and culture; (3) chest roentgenography; (4) electrocardiography; determinations of (5) blood urea or blood urea nitrogen, (6) serum creatinine, (7) serum calcium and phosphorus, (8) blood uric acid, (9) serum sodium, potassium, and bicarbonate, (10) 24-hour urinary protein; and (11) a flat plate of the abdomen for kidney size.

If there is any suggestion of urinary obstruction, I obtain an infusion excretory urogram. The patient need not thirst prior to this examination. Patients with multiple myeloma or severe diabetic nephropathy are most liable to exhibit a decrease of renal function after contrast studies. If an excretory urogram is necessary in such a patient, normal fluid intake should precede the test and I measure the urinary volume and determine the serum creatinine concentration after the examination.

I usually measure a 24-hour creatinine clearance using the same urine specimen collected for determination of 24-hour protein loss. If the creatinine clearance is not measured, it can be estimated from the serum creatinine concentration (mg/dl). In an average-sized man, 100/serum creatinine approximates creatinine clearance. In an average-sized woman, the creatinine clearance can be estimated by 70/serum creatinine.



Figure—Distal brown arcs just proximal to free edge of fingernails. The nails are pale otherwise and without half moon.

Treatment

Treatment is begun after reversible causes of renal failure have been ruled out. It includes optimal sodium, protein, and calorie intake, as well as specific medications.

The sodium prescription depends on estimates of total body sodium and current sodium intake. First, if a dietitian is not available to obtain a thorough account of the patient's current dietary intake, you can make a rough estimate of sodium intake from simple indications: The patient who adds no salt at the table and who avoids obviously salty foods usually consumes 90 to 100 meq of sodium per day; and the patient who eats salty foods and salts food liberally, often before tasting, consumes 200 or more meq of sodium per day. You must also estimate the ECFV, which is determined by the total body content of sodium. (This estimation of ECFV is a clinical evaluation. The serum sodium concentation per se does not reflect total body sodium.)

If the ECFV is expanded—the sodium intake must be reduced. I often begin with 40 to 90 meq (1 to 2 g) of sodium per day. If 40 meq per day proves excessive, I usually add furosemide, 80 mg or more in a single dose, every other morning rather than reduce the sodium intake further.

If the ECFV is depleted—the sodium intake is increased. Also, if the ECFV is normal and the diastolic blood pressure is less than 100, the sodium intake is increased but more cautiously. This balance between sodium intake and ECFV is not static; it must be reassessed frequently.

The appropriate intake of protein and total calories depends on the renal function and the presence or absence of uremic symptoms (anorexia, nausea, vomiting, muscle-twitching, and weakness). To start with, I recommend: 0.5 g protein per kg body weight per day if the creatinine clearance is between 20 and 30 ml/min, or 0.38 g protein per kg body weight per day if the creatinine clearance is 5 to 19 ml/min, or 0.26 g protein per kg body weight per day if the creatinine clearance is less than 5 ml/min.[3] An amount equal to the 24-hour urinary loss of protein is added to the calculated protein prescription. I ask the patient to take 1 multiple-vitamin capsule daily. The protein intake can be adjusted if uremic symptoms do not improve after several weeks. Few patients are asked to eat the lowest amount of protein prescribed (0.26 g/kg per day) for more than a few weeks if chronic repetitive hemodialysis or renal transplantation is available.

The dietitian must emphasize the intake of foods with proteins of high biologic value (proteins with the greatest content of essential amino acids) such as egg, milk, meat, fish, and fowl. If enough nonprotein foods are eaten (2,000 to 3,000 calories per day), along with adequate essential amino acids, the body can use urea nitrogen in the production of nonessential amino acids.[4] If the intake of either nonprotein foods or essential amino acids is inadequate, the body will utilize the amino acids for energy. This leads to increased levels of nitrogenous waste products.

When the creatinine clearance is less than 25 ml/min, the serum phosphorus concentration usually is elevated; and by that time the intestinal absorption of calcium is depressed. The combination of elevated serum phosphorus and suboptimal calcium absorption leads to secondary hyperparathyroidism. This condition—characterized by increased serum parathyroid hormone levels—may lead to cystic bone changes and osteomalacia with or without bone pain and fractures. In an effort to minimize secondary hyperparathyroidism, I recommend oral phosphate binders such as Amphojel or Basaljel, 30 ml three or four times daily, and added calcium after the serum phosphate is less than 6.0 mg/dl and after the product of the serum phosphorus (mg/dl) times the serum calcium (mg/dl) is less than 70. (When the product is greater than 70, soft-tissue calcification is likely.) For such calcium supplementation I prefer powdered calcium carbonate, one level measuring tablespoon in water or soda pop 30 minutes before breakfast. This amount of powdered calcium carbonate supplies approximately 2 g of calcium per day, and base as well.

If the serum uric acid level is high, allopurinol, 50 mg three times a day, may be given by mouth.

After beginning this treatment, I ask the patient to return in two to three weeks. The determinations of serum creatinine, blood urea or blood urea nitrogen, serum calcium, and serum phosphorus are repeated. I discuss the diet and medications and re-estimate the ECFV. If possible, the dietitian should talk with the patient again. The most common change is in the prescription of dietary sodium.

There are three observations the patient can make for guidance in minimizing depletion or excessive accumulation of sodium: body weight, daily; supine and standing blood pressure, twice daily; and leg edema. If any one of these three varies from the patient's base-line observations, or if the patient cannot eat the entire diet or loses fluids excessively (by vomiting or diarrhea), he should notify his physician promptly. Viral gastroenteritis with vomiting or diarrhea often requires a brief hospital admission for intravenous administration of saline.

When the serum creatinine rises above 6 to 8 mg/dl, you must consider eventual repetitive hemodialysis or renal transplantation. The patient should then be seen at a dialysis-transplantation center at least once. Thanks to the foresight of Minnesotans (physicians, social workers, legislators, and interested lay groups), dialysis or renal transplantation is available to nearly every patient who needs it.

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At length, PEEL is called in "in a regular way." Being assured of his quarterly fee, the state physician may now, in the magnanimity of his soul, prescribe new life for moribund John Bull. Whether he has resolved within himself to emulate the generous dealing of kindred professors—of those sanative philosophers, whose benevolence, stamped in modest handbills, "crieth out in the street," exclaiming, "No cure, no pay,"—we know not; certain we are, that such is not the old Tory practice. On the contrary, the healing, with Tory doctors, has ever been in an inverse ratio to the reward. Like the faculty at large, the Tories have flourished on the sickness of the patient. They have, with Falstaff, "turned diseases to commodity," their only concern being to keep out the undertaker. Whilst there's life, there's profit—is the philosophy of the Tory college; hence, poor Mr. Bull, though shrunk, attenuated—with a blister on his head, and cataplasms at his soles—has been kept just alive enough to pay.*

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*"Peel 'Regularly Called In':" Punch, 1841.

Minnesota State Medical Association

121st Annual Meeting of the Minnesota State Medical Association will be held in Duluth, May 16 and 17, in the Duluth Arena-Auditorium.

Headwaters Clinical Conference

The Third Annual Headwaters Clinical Conference has been scheduled for Friday, June 21, 1974, at Ruttger's Birchmont Lodge in Bemidji, Minnesota. The theme for the discussion will be "Pediatric Medical/Surgical Problems in General Practice." For detailed information and advance registration cards contact Headwaters Clinical Conference Committee, Bemidji Hospital, Bemidji, Minn. 56601.

Renal Lithiasis

An Optimistic Outlook

DAVID M. WILSON, M.D.;* LYNWOOD H. SMITH, M.D.;* JOSEPH M. SEGURA, M.D.†
and REZA S. MALEK, M.D.†

Evaluation of the etiology of renal stones allows for a rational approach to therapy. For most types of renal stones medical therapy is effective in preventing further growth.

Man has been plagued with kidney stones since history began, and they are among the more common of his medical afflictions. Our clinic receives more than 1,500 cases of kidney stone yearly; that is, renal lithiasis is diagnosed in two of every 300 patients seen. Yet the factors that underlie stone formation have been poorly understood, and until recently the therapy has been very unsatisfactory. Consequently our divisions of nephrology and of urology joined efforts some time ago to study the metabolic as well as surgical factors important in the management of patients with renal lithiasis.

A simple classification that will serve our purpose for this report has four categories: (1) uric acid stones, (2) infected stones, (3) cystine stones, and (4) calcium metabolic stones. In describing the origin, diagnosis, and management of these problems we shall give most attention to calcium metabolic stones and especially the idiopathic subcategory, which is thought to comprise 60 to 80% of all cases of renal stone; but a few comments on the first three categories are in order.

Uric Acid Stones

Uric acid lithiasis is second only to calcium stones in frequency in this country. About 50% of patients with uric acid lithiasis have hyperuricemia or hyperuricosuria, suggesting that other factors such as persistent low urinary pH may be very important. These patients commonly present with acid urine or low urinary volume. A defect in ammonia production in gout has been proposed to explain the acidity of urine in that disease. Many patients with problems other than gout also have persistently acid urine, however, such as those with chronic diarrhea or ileal diversion of the urinary tract, and those who—after ureterosigmoidostomy—have bicarbonate wasting from the bowel and consequently are persistently acidotic and produce urine of both low pH and low volume. Many patients who have primary bowel disease with diarrhea also tend to be acidotic and have acid urine. It is not uncommon to find uric acid stones in gouty or hyperuricemic patients who have been treated with uricosuric agents that decrease plasma urate at the expense of increasing urinary uric acid.

Uric acid stones may occur in patients with hyperparathyroidism, and increased uric acid excretion has also been implicated in the production of calcium kidney stones in idiopathic renal lithiasis. It has been reported that as many as 12% of the stones formed by patients with gout are calcium kidney stones, and that there is a high incidence of hyperuricemia, or hyperuricosuria in patients with calcium kidney stones. There are even some reports suggesting that suppression of hyperuricosuria may benefit patients who form calcium kidney stones.[1]

The diagnosis of uric acid stones depends upon the characteristic x-ray appearance of a radiolucent stone that may be branched or staghorn. When uric acid stones are large they may contain calcium or heavy-metal impurities, and a few may be somewhat radiopaque.

Treatment includes administration of alkali—such as sodium bicarbonate or a citrate solution (Polycitra)—to keep the urinary pH at 6.5; and allopurinol can be added while the stones are being dissolved.

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See editorials, page 390.

Infected Stones

When infection is added to renal lithiasis, the problem is challenging indeed; and nowhere is the need for cooperation between the surgeon and internist more important. In our series more than 50% of such cases include some metabolic abnormality that contributes to stone formation.[2] The cause must be identified in order to prevent further lithiasis, even if the current problem is controlled.

Most infected kidney stones are composed of magnesium, ammonium phosphate, or struvite; there are reports of infection in calcium phosphate stones. The overwhelming majority of patients with infected struvite stones have *Proteus* bacteriuria; but when the infection is with other bacteria, it often is difficult to tell whether the infection is in the stones or only associated with them. Most often infections with species of *Escherichia coli* or other organisms that do not split urea, though associated with stones, do not infect them. Many stones recognized radiologically as infected are branched or staghorn, but obviously some infected stones are not of this characteristic shape. Some infected stones are mottled or varied in radiodensity, and this feature may distinguish them from other staghorn calculi such as cystine stones with a ground-glass appearance or the more radiolucent urate stones.

The distinction between infection within renal stones and urinary-tract infection only associated with other types of metabolic stones (such as calcium oxalate) is important, since fewer than 5% of infections within stones can be eradicated by antibiotics alone. One can expect to clear the infection in more than 80% of cases by complete removal of the infected stone material in conjunction with careful antibiotic control and long-term suppression with appropriate follow-up.

Cystine Stones

Cystine stones may be confused with calcium stones, since—contrary to some reports—they are radiopaque. They may be solitary, multiple, or branched; and they may have a ground-glass appearance. The diagnosis of cystine stones is strongly suggested by excess cystine in the urine, as revealed by the nitroprusside test or by quantitative amino acid analysis. The nitroprusside reaction is very sensitive and also may identify heterozygote carriers of the gene for cystinuria in some patients.[3] These carriers usually excrete less than 400 mg of cystine per liter of urine and rarely, if ever, have cystine stones, since cystine is soluble to at least 300 mg/liter, depending on urinary pH. Ordinarily the distinction between cystinuric patients and carriers can be made by use of quantitative amino acid analysis. The treatment for cystine stones depends on maximal alkalinizing of the urine, since the solubility of cystine does not increase much until the pH is greater than 7.0. A program to produce a consistent increase in urinary volume, including drinking at night, is imperative for these patients; and some may require D-penicillamine with its attendant dangers in order to control the stones. Unless there is complete obstruction of urinary flow or the kidney is so badly damaged that there is virtually no urinary output, medical control usually can be achieved and surgery may not be necessary for this type of stone.

Calcium Metabolic Stones

After exclusion of the three categories mentioned above, one is confronted with a group of stones composed principally of calcium apatite or calcium oxalate, or most commonly a mixture of calcium apatite and oxalate.

An etiologic classification of the majority of these stones is in Table 1. This is somewhat

TABLE 1

Etiologic Classification of Calcium Metabolic Renal Stones

- Alkaline urine
  - Distal RTA (type 1)
  - Carbonic anhydrase inhibitors
  - Excess intake of absorbable alkali
- Hyperoxaluria
  - Primary
    - Type 1 (glycolic aciduria)
    - Type 2 (L-glyceric aciduria)
  - Acquired hyperoxaluria with gastrointestinal disorders
  - Hypervitaminosis C
- Hypercalcemia
  - Primary hyperparathyroidism
  - Hypervitaminosis D
  - Sarcoidosis
  - Milk-alkali syndrome
  - Cushing's syndrome, hyperthyroidism
  - Malignancy
  - Immobilization
- Idiopathic
  - Excess of crystalloid (activity product)
  - Deficiency of inhibitor activity

arbitrary but serves to orient the approach to diagnosis and therapy in a more rational way.

From 60 to 80% of all calcium kidney stones are idiopathic. It is evident that this is a diagnosis of exclusion, and it is therefore important to recognize the known forms of calcium renal lithiasis, since many of the known causes of calcium metabolic stones are amenable to specific therapies.

Known Causes

Alkaline Urine.—Renal tubular acidosis (RTA) is the classic form of this problem. Patients with RTA have several reasons for renal lithiasis. They have alkaline urine and decreased citrate excretion; and when acidotic, many of them have hypercalciuria. Not all of these patients have systemic acidosis, but all have a persistently alkaline urinary pH that may promote in particular the formation of apatite or calcium phosphate stones. A first-morning urinary pH less than 5.5 excludes this as a cause, but sometimes 100 mg of NH_4Cl per kilogram of body weight must be given and the urinary pH tested four to eight hours later. A value greater than 5.5 substantiates a form of RTA in the presence of systemic acidosis. This may be difficult to determine in patients with an infected urinary tract, since urea-splitting organisms may elevate the urinary pH and other bacteria may produce acid and thus lower it.

About 70% of patients with type 1 (distal) RTA have nephrolithiasis or nephrocalcinosis, but in our experience overt RTA is rare among patients with urolithiasis. Pure type 2 (proximal) RTA has not been reported in association with kidney stones. The distinction between patients with distal and proximal RTA can usually be made easily, since proximal RTA is often associated with other tubular abnormalities such as aminoaciduria, hyperphosphaturia, uricosuria, or potassium wasting. Many patients excrete alkaline urine consistently even though they have no intrinsic renal problem.[4]

Patients may excrete excess alkali in the urine for various reasons resulting from either metabolic or respiratory alkalosis. Many patients with upper-gastrointestinal complaints take absorbable alkali, which is often in combination with calcium; and both of these substances promote formation of stones. Some patients take diuretics that may produce hypokalemic alkalosis, and of course many patients who take acetazolamide (Diamox) excrete alkaline urine for a long period: kidney stones are not uncommon in these circumstances.

Hyperoxaluria.—Excess of oxalate in the urine increases the possibility of stone formation. Relatively small increases in urinary oxalate may be important in stone formation, so urinary oxalate even in the high normal range (30 to 40 mg/24 h) may exceed the solubility for oxalate.

Urinary oxalate may be increased as a result of an error in metabolism, altered gastrointestinal absorption, or even drug ingestion. There are two forms of familial hyperoxaluria, both probably inherited in a recessive autosomal manner. And a secondary form of hyperoxaluria has been described that may be much more common. Patients with bowel disease—frequently those with a significant portion of ileum removed—may have hyperoxaluria because of an alteration in bile acids.[5] These patients apparently absorb a much larger proportion of ingested dietary oxalate. It has been thought that absorption of dietary oxalate contributed only a small proportion to the oxalate excreted by persons without bowel disease, but recent reports suggest that oxalate unassociated with calcium, as it is in tea, may be absorbed more easily even by normal individuals. It has also been reported[3] that ingestion of large doses of vitamin C may increase excretion of oxalate. The treatment for secondary hyperoxaluria appears to be restriction of the ingestion of oxalate. The treatment of patients with primary hyperoxaluria and stones is exceedingly difficult. Many respond to large doses of neutral phosphate, and pyridoxine may lessen the urinary oxalate in some cases.

Hypercalcemia.—Usually hypercalcemia is easy to identify, although the variability in measurement of calcium often results in confusion as to whether a state of hypercalcemia exists. Atomic absorption flame photometry in our laboratory gives 10.2 mg/dl for the upper limit of normal, and among older patients the upper limit may be actually lower than this.[6] Often two or three determinations are necessary to establish the calcium level, since severe dehydration, enemas, etc., may raise the serum concentration and drugs such as thiazides may elevate it for as long as three to four weeks. Some laboratories list upper limits as high as 11 mg/dl, causing doubt as to whether the difference is in their methods or in their definitions of normal. The serum calcium value is still the most reliable for suggesting primary hyperparathyroidism.

We have seen very few normocalcemic (<10.2 mg/dl) patients with hyperparathyroidism, but 31% of our patients with hyperparathyroidism had serum calcium values between 10.1 and 10.9.[7] A very small group of women with hypercalciuria and stones but only borderline-high serum calcium values had parathyroid adenomas.[8] Of our primary parathyroid patients 51% had kidney stones, but only 11% had had new stone formation or increase of stone size over at least a year's observation, which we classified as "metabolically active" kidney-stone formation.[7] Virtually all these patients quit forming stones after removal of the adenoma, although rarely calcium excretion may actually rise and stone formation continue after removal of a parathyroid adenoma. Neutral phosphate can be used successfully if removal of the adenoma cannot be accomplished.

In addition to those factors already discussed, hypercalciuria may be associated with active osteoporosis, Paget's disease, beryllium ingestion, and multiple myeloma. Often patients taking vitamin D have excess serum calcium, but they may have hypercalciuria even if the serum calcium is in the normal range. Nephrocalcinosis also is seen in this situation. And hypervitaminosis D may result in RTA. Sarcoidosis may be associated with hypercalciuria or hypercalcemia, as are immobilization and ingestion of large amounts of calcium, particularly when there is some renal impairment. Cushing's syndrome and hyperthyroidism cause hypercalciuria and sometimes stones. The coincidence of kidney stone and malignancy in hypercalcemic patients is rare but does occur.

Idiopathic Calcium Metabolic Stones

Since the large majority of calcium kidney stones are idiopathic, it is fortunate that therapy is very successful in preventing stones of this kind. This has become possible through increased understanding of many of the multiple factors involved in stone formation.

Etiologic Possibilities.—We have divided the cases of idiopathic calcium stones into those with excessive crystalloid constituents in the urine and those without such excess. This classification is arbitrary, and there may be influence from several factors that promote stone formation by increasing the *activity* (or form of the crystalloid available to precipitate) of those constituents in the urine. Clearly, however, the concentration or amount of crystalloids in the urine is not the only factor. At least 10% of the presumedly normal population have excess calcium in the urine and yet no kidney stones. In our series of patients with idiopathic renal lithiasis, only 50% had increased urinary calcium (>275 mg/24 h for men and >250 for women, on a diet including at least one quart of milk a day).[9,10] Furthermore, although many patients with hyperparathyroidism have stones, just as many of the patients with hyperparathyroidism have hypercalciuria but not stones.

Between 50 and 80% of patients with idiopathic renal lithiasis do have hypercalciuria for which no cause is apparent. Albright et al.[11] coined the term "idiopathic hypercalciuria" to describe the syndrome of renal stone formation with high urinary calcium excretion, normal serum calcium concentration, and frequently low plasma phosphorus concentration.

The possible mechanisms leading to hypercalciuria are of two primary kinds: a defect in reabsorption of filtered calcium in the kidney, with resultant excess excretion;[12] and a primary increase in the intestinal absorption of calcium.[13] Which of these is more important has not been settled. The observation that some of these patients have a negative calcium balance, particularly when calcium intake is limited, favors a compelled renal loss of calcium. Many patients with idiopathic hypercalciuria (IHC) continue to excrete an inappropriately large amount of calcium in urine despite ingesting none or nearly none. If the hypercalciuria were due to overabsorption by the intestine, one would expect a return to normality when calcium absorption was restricted. Coe et al.[14] recently reported that the parathormone concentration was high in the majority of their patients with stones and hypercalciuria, and that this concentration became normal after thiazide administration, which among other things decreases urinary calcium and supports the concept of primary renal wasting of calcium. Edwards and Hodgkinson[12] examined renal calcium reabsorption and found that reabsorption of calcium from the renal tubule is less than normal in IHC patients. This would also fit the original proposal by Albright et al.,[11] who believed that renal tubular damage led to decreased renal reabsorption of filtered calcium and hypercalciuria.

Other studies of some of the same factors cited above have given quite different results that suggest increased intestinal absorption of calcium. Some studies of renal excretion of calcium revealed no abnormality of renal calcium threshold or tubular reabsorptive capacity.[15] Most studies of calcium metabolism in patients with IHC show increased absorption of calcium with decreased fecal excretion of it. Pak et al.[13] observed that intestinal absorption exceeded urinary excretion in all their patients with IHC and suggested that hyperabsorption could fully account for it. In favor of increased absorption are the observations that these patients do not have evidence of calcium depletion such as bone disease. Furthermore, a kidney donated by a patient with IHC was not hypercalciuric after transplantation.[16] In contrast to the data of Coe et al.,[14] data from our patients with hypercalciuria show very few have increased parathyroid hormone values. Most have normal or low values, an observation that may support the concept of increased intestinal absorption in a majority of patients. It seems likely that hypercalciuria may be a result of either or both of these phenomena in different patients or circumstances; and furthermore, increased absorption leading to hypercalciuria could result eventually in renal damage and consequent renal calciuria.

Studies to elucidate why either increased excretion or increased absorption may occur are meager and speculative. Hypercalciuria has been reported with diseases that result in renal tubular damage, such as Wilson's disease, Fanconi's syndrome, and renal rickets; but no other tubular abnormalities in patients with IHC have been reported and there are no models of isolated calcium wasting.

Patients with sarcoidosis have hypercalciuria and have been shown to be hyperresponsive to administration of vitamin D. Some studies have shown that vitamin D produces more increase of urinary calcium in IHC patients than in controls,[16] while other studies have shown no such increase. Against vitamin D as etiologic in this syndrome is the fact that administration of steroids lessens the urinary excretion of calcium by patients with sarcoid and vitamin D intoxication but does not affect it in patients with IHC.[12]

Related Therapeutic Considerations.—Although the cause of the hypercalciuria in these patients has not been clearly established it seems quite likely that multiple factors will be identified eventually and that, indeed, some patients may have primary hypercalciuria with a negative calcium balance while others may have increased calcium absorption that results in compensatory hypercalciuria. The treatment for this syndrome over the long term may depend on this determination, since to restrict ingestion of calcium by a patient who is wasting it from his kidney may result in calcium depletion. On the other hand, to decrease renal excretion of calcium with drugs such as thiazides may be harmful in the long run to those patients in whom increased absorption of calcium is primary. We now have several different modalities for treating these patients and hope to be able to adapt the methods to the causes. For example, to restrict calcium intake or give drugs such as cellulphosphate (which binds calcium in the intestine) would be appropriate in cases of increased intestinal absorption.

Thiazide diuretics have been used to reduce calcium excretion and have been reported to decrease kidney stone formation in about 70% of patients with hypercalciuria actively forming stones. Cellulose phosphate has been used experimentally to lessen calcium absorption but is not available for general use in this country.

Other crystalloids also may reach excessive concentrations in the urine and promote stone formation. We have discussed increased oxalate in the urine and the factors that may promote oxalate excretion. It is probably not effective to restrict dietary oxalate in cases of oxalate stone unless there is clearly abnormal absorption of oxalate (for example in bowel disease) although it is not clearly established that dietary restriction is always ineffectual.

The form of a particular species such as calcium or oxalate in the urine is important—that is, whether it is in a form that will precipitate in a stone. The solubility of calcium phosphate, for example (and the solubility of magnesium ammonium, cystine, and uric acid as well), depends on urinary pH. Calcium phosphate stones are more likely to precipitate in urine that is alkaline. Calcium oxalate, however, is essentially insensitive to changes of urinary pH within the physiologic range. Yet pH may be important even n calcium oxalate stone formation, since oxalate stones are often mixed with apatite, which is pH-sensitive. Because of a possibility that oxaate may precipitate on uric acid crystals that are pH-sensitive, allopurinol has been given to some patients who had calcium stones,[1] particularly to those with hyperuricosuria; but this is not an established mode of therapy at the present ime.

Yet pH may not be the only determinant of whether crystalloids may precipitate in urine. Those patients whose urinary calcium, oxalate, and phosphate are in the normal ranges still have enough crystalloid so that in many circumstances stones or crystals would precipitate if in water or physiologic salt solution; yet stones do not orm in most people. There are several constituents of urine known to inhibit precipitation of calcium crystals. These include citrate, magnesium, and pyrophosphate, each of which works in a different way to prevent crystallization. Although abnormalities of these factors could result in stone formation, they are not abnormal in patients with idiopathic renal lithiasis. However, several workers have reported an unidentified inhibitor hat has been shown to prevent crystal growth and is decreased in the urine of some patients with idiopathic renal lithiasis.[17] The exact nature of this inhibitor[5] is not yet known, but it is the subject of intense investigation.[18]

Treatment

Despite all the uncertainties mentioned, the treatment for renal lithiasis can be remarkably effective. Several programs of treatment for stones have attempted to increase inhibitor activity in urine. Magnesium oxide has been reported to decrease stone formation. Neutral phosphate therapy increases pyrophosphate excretion and decreases calcium excretion. Increased phosphorus and decreased calcium excretion from neutral phosphate result in little change in the activity product of Ca x PO_4, but the increase of inhibitory activity with appropriate doses (1.6 to 2 g elemental phosphorus or more) has been the most effective form of treatment for idiopathic calcium stones, whether the patients are hypercalciuric or not. In our clinic we have stopped stone formation in 95% of patients with idiopathic renal lithiasis.[10] About two-thirds of the cases we see are not included in this statistic, however, because—given only the advice to increase oral intake of fluid to 12 glasses per day and to restrict intake of dairy food—they form no stones thereafter. We have therefore adopted a policy of treating only patients with metabolically active stones.[19] This we define as stone growth within the past year, formation of a new stone within the past year, or demonstrated passage of gravel within the past year. Of course, the surgical approach to stones depends on other criteria, and we define a surgically active stone as one producing colic, obstruction, or infection requiring surgical intervention. We try to identify the known causes of stones and deal with those factors whenever possible. Modes of therapy may be selected from a wide variety available (Table 2), which must be tailored to the pathogenesis and clinical condition of each patient. We have prescribed neutral phosphate for most patients with idiopathic active renal lithiasis, but thiazides for some with marked hypercalciuria. Long-term evaluations of the kidneys by roentgenography, with or without tomograms, are the benchmarks of a successful treatment program, since various actions or advice may be necessary.

TABLE 2
Renal Lithiasis: Available Therapeutic Measures and Mode of Effects

Agents used	Effect
Fluids	Decreases solute load
Restriction of Ca, PO_4, oxalate intake	Decreases solute load
Thiazides	Decreases solute load
Inorganic phosphate	Decreases urinary calcium Increases pyrophosphate ?
Cellulose phosphate	Decreases calcium absorption
Methylene blue	Crystal poison (matrix)
Acid loading (NH_4Cl, cranberry juice, etc.)	Increases solubility of apatite and struvite
Allopurinol	Decreases uricosuria
Magnesium	Competes with calcium
Pyridoxine	May lessen oxalate load
Alkali ($NaHCO_3$, Polycitra, etc.)	Increases uric acid and cystine solubility

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See references, page 423.

Anemia of Renal Failure

A Review

JOSE A. DIAZ-BUXO, M.D.* and PETER P. FROHNERT, M.D.*

A multitude of exogenous and endogenous factors are involved in the etiology of anemia of chronic renal failure, most of which are correctable by careful conservative management. Since even severely atrophic kidneys have substantial influence in the regulation of erythropoiesis, bilateral nephrectomy should not be performed routinely unless specific indications require such a procedure.

RENAL DISEASE frequently is associated with hematologic disorders. Simple cysts, or polycystic renal disease, as well as hypernephroma and hydronephrosis, may produce polycythemia; and acute renal failure occasionally may be associated with red-cell aplasia.[1,2] Anemia usually develops in progressive renal insufficiency and often is its major presenting feature.[3] Although other symptoms of renal failure ordinarily are well controlled by chronic intermittent hemodialysis, the conventional form of this treatment has not much effect on anemia of chronic renal failure.

In this paper we shall review causes of anemia in chronic renal failure and outline therapeutic programs, with particular emphasis on recent developments.

Causes of Anemia in Chronic Renal Failure

Blood Loss

Uremia affects blood coagulation through several mechanisms, including the inducement of platelet defects, and thus increases the tendency to bleed and the possibility of massive gastrointestinal hemorrhage and extensive ecchymosis. Blood loss can be more subtle but still substantial if it occurs on a chronic basis, as during intermittent hemodialysis. Here, small amounts of blood are left behind in the dialyzer at the end of each treatment. The amount of loss (15 to 30 ml/dialysis) depends greatly on the type of dialyzer used and the care with which blood is returned to the patient at the end of dialysis. Greater losses occur when a dialyzing membrane ruptures or when poor blood flow or inadequate heparinization leads to clotting within the dialyzer. Depending on the type of dialysis system, up to 300 ml of blood may be lost by such an event. The physician himself may contribute substantially to the anemia of renal failure through necessary and unnecessary sampling of blood for laboratory work. It is easy to calculate that the dialysis patient may lose more than 3,500 ml of blood annually by dialysis-related events alone.

Hemolysis

The peripheral blood smear of patients with renal failure occasionally suggests hemolysis. Indeed, a shortened erythrocyte life span has been a consistent finding of several studies.[4-13] The severity of hemolysis is variable and correlates best with the impairment of renal function. Incubation of uremic erythrocytes in normal plasma produces no significant hemolysis. Contrariwise incubation of normal red blood cells in uremic plasma stimulates hemolysis. This strongly suggests that the hemolysis of chronic renal failur is due to extracorpuscular factors.[6-8,12] In som severely uremic patients, the red cells themselve are affected; and their survival after transfusio into normal subjects is briefer than usual.[12,1] The nature of the extrinsic factor or so-calle toxin is not yet determined, but its plasma clearance and its renal handling resemble those o phosphate and uric acid.[12] Its mode of action i likewise indeterminate, but may involve altera tions in red-cell enzyme activity, transmembranous ion transport, or organic phosphate content.[15-20] Giovannetti et al.[21,22] were able to show that the BUN level had no effect on red-cell survival, but hemolysis was induced by addition of guanidine, creatinine, and creatine to normal red cells.

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In general, there seems to be no abnormal sequestration of red cells in the liver or spleen. The fact that several patients with hemolytic anemia of renal failure improved after splenectomy[23-26] certainly indicates that the spleen removed defective erythrocytes but does not necessarily prove that "hypersplenism" was the cause of the hemolytic anemia.[27]

Some exogenous hemolytic toxins may be inadvertently introduced in the dialysate. Copper from water piping,[28,29] nitrates from well water,[30] and chloramines from city water[31] have caused clinically significant hemolysis and required particular ingenuity for their identification and elimination. The Figure shows major glycolytic pathways in the erythrocyte. Since the red blood cell has no mitochondria, only anaerobic processes are available for the production of energy-rich phosphates. The hexose-monophosphate shunt accounts for only 10% of red-cell glycolysis; but it is of paramount importance because it generates NADPH, which protects hemoglobin against oxidizing agents. Chloramines seem to reduce the hexose-monophosphate shunt besides oxidizing hemoglobin directly, thus inactivating hemoglobin in two ways.[31]

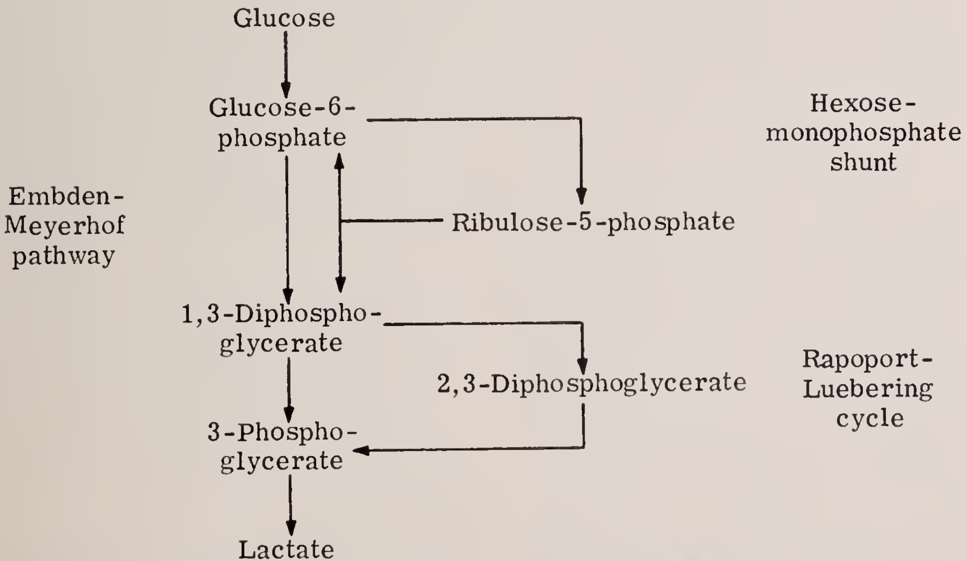
Mechanical factors are of minor importance in the hemolytic process of renal failure. Microangiopathic anemia has been observed in severe and poorly controlled hypertension. Mechanical hemolysis like that in cardiopulmonary bypass procedures seems to occur to some extent during hemodialysis, but studies of Frost et al.[32] showed that its amount is negligible.

Erythropoiesis

Extrinsic Factors.—Although iron-binding capacity is low in many cases of chronic renal failure,[4] lack of plasma iron is due mainly to a negative iron balance caused by the excessive losses described above. Gastrointestinal reabsorption of iron appears to be normal in these circumstances,[33] or even increased in the presence of iron deficiency.[34] Restriction of dietary protein and potassium often results in a diet that is low in iron content, and indeed deficient if one considers concurrent iron losses.

For similar reasons, inadequacy of dietary supply may cause depletion of hematinic vitamins—folic acid in particular—resulting occasionally in a classic pattern of megaloblastic anemia. Hemodialysis again may aggravate the situation by removing the water-soluble vitamins from the body.

Erythropoietin.—Although blood smears in renal failure may be macrocytic, microcytic, or microangiopathic, the most frequent finding is that of normocytic, normochromic anemia. This occurs regularly when renal function, as meas-



Figure—Glucose metabolism in the erythrocyte. Only major pathways are represented, and they are in simple form.

ured by inulin or creatinine clearance, declines to 20% of normal or lower.[35] In that situation, bone-marrow studies show hypoproliferation of the erythroid series and little response to powerful erythropoietic stimuli such as hypoxia and decreased red-cell mass.

These findings and the observation that the bone marrow responds normally after transplantation suggested participation of the kidneys in normal hematopoiesis. Systematic extirpation of intra-abdominal organs pointed to the kidneys as the only organ capable of producing enough of the principle named "erythropoietin" to prevent development of severe anemia. Recently Busuttil et al.[36] have suggested the epithelial cells of the glomerular tuft as the site of erythropoietin production. Their proposal was based on localization of fluorescent anti-erythropoietin in the hypoxic dog kidney, a finding in agreement with the observation by Burlington et al.[37] that erythropoietin was produced in cultures of goat glomeruli.

Although clinical data supported the dominant role of the kidneys in erythropoietin production, it was soon established that the kidney is not the only source of erythropoietin, since anephric patients in many series have shown circulating erythropoietin[38-45] and an appropriate response, albeit depressed, to extreme anoxia. It is not clear from the available data whether the defect in responsiveness is due to inhibition of erythropoietin activity, end-organ unresponsiveness, or accelerated inactivation of erythropoietin; but it seems likely that the most important determinant is defective renal production of the erythropoietic factor, due to loss of renal parenchyma.

Red-Cell Abnormalities and Adaptive Mechanisms

An interesting concept in the etiology of the anemia of chronic renal failure has been advanced recently by von Hartitzsch and co-workers.[46] They observed that in tissues where oxygen pressure was low, synthesis of red-cell 2,3-diphosphoglycerate (2,3 DPG) was enhanced and hemoglobin-oxygen affinity was decreased, with consequent greater release of oxygen. On that basis they proposed that the anemia of renal failure may reflect the lack of hypoxic stimulus and not inability to produce erythropoietin—in other words, that anemia is a normal response of the organism to altered conditions of oxygen delivery. This hypothesis builds on work of Benesch and Benesch[47] and Chanutin and Curnish,[48] who showed that intra-erythrocytic concentrations of organic phosphates, namely 2,3 DPG and adenosine-triphosphate (ATP), reduce the oxygen affinity of hemoglobin significantly. 2,3 DPG is the product of a shunt in the glycolytic pathway of the red cell (Figure) and comprises 70% of the organic polyphosphates in the erythrocytes. It binds to the beta chains of deoxygenated hemoglobin, thereby impeding the oxygen uptake of the hemoglobin. Increased levels of 2,3 DPG have been demonstrated in anemia, cardiac and respiratory insufficiency, high-altitude sickness, and renal failure.[49-54] The intracellular concentration of organic phosphate seems to correlate well with the serum concentration of inorganic phosphate, as evidenced by decreased erythrocytic 2,3 DPG and ATP concentration and increased oxygen affinity during hypophosphatemic states.[55-57] Blumberg and Marti[58] also found some of these correlations in their patients with hyperphosphatemia of renal failure.

Treatment for Anemia of Chronic Renal Failure

General Measures

The prevention of blood loss is of utmost importance in cases of renal failure, as implied above. Therefore, uremia requires aggressive and early treatment to curb the tendency to hemorrhage in renal insufficiency. Quite often, this may entail dialysis. The dangers of blood loss due to the procedure itself are well recognized by everyone involved with this form of therapy, and certain accidents such as leaks in the dialyzer membrane will continue to happen. But blood loss due to excessive laboratory work is an avoidable complication that usually can be charged to inexperience. Intensive training and thorough peer review can greatly reduce losses due to this problem.

A recent study from the University of Minnesota[27] showed normal survival of ^{51}Cr-labeled red cells in 11 well-dialyzed patients, of whom 3 had been nephrectomized. The authors asserted that previously reported failures of hemodialysis to normalize red cell survival[59,60] were probably due to inadequacy of the dialysis. Success depends only in part on the duration of the process and the area of dialyzing membrane.[61] In hemolytic anemia the purity of water and absence of toxic contaminants are also critical.[28-31,62] Various measures, such as avoidance of copper pipes and addition of ascorbic acid to the dialysate, help to prevent dialysis-related hemolysis.

Iron and vitamin supplementation are prescribed routinely in almost all dialysis units and are strongly recommended for the anemic patient in renal failure who lives on a severely protein-restricted diet. It is important to choose vitamin preparations that include not only vitamin B_{12} but also folic acid, particularly for the patients undergoing dialysis. Serum iron concentrations should be monitored routinely, and sufficient iron should be administered orally to bring the values into the normal range.

Androgen Therapy

Androgens have long been known to increase hematopoiesis in rodents[63] and in man.[64] Several investigators demonstrated that these substances can alleviate anemia of chronic renal failure also. [47,65-67] In 1967 Alexanian and co-workers[68] proved that androgenic hormones increased the excretory rate of erythropoietin in 22 normal subjects. Two years later Mirand and associates[41] showed that androgens stimulated erythropoietin production in anephric men and suggested that in man the extrarenal production of erythropoietin, like the renal production, responds to exogenous testosterone. Recently Eschbach and Adamson[66] reported that three to six months of androgen therapy improved erythropoiesis significantly in 13 of 14 patients, as reflected by reduction of need for transfusions and increase of blood mass. The improvement in erythropoiesis was proved by the turnover of erythroid iron. It was accompanied usually by either an increase in measurable serum concentrations of erythropoietin or a reduction in the mean marrow-transit time of iron, suggesting that the androgens acted primarily by stimulating erythropoietin production. The response was not dependent on the presence of residual renal tissue, and the amount of androgen used was not significantly toxic.

That androgens have a positive erythropoietic effect in at least some patients with the hypoproliferative anemia of chronic renal failure seems well established. There is good evidence that production of erythropoietin is enhanced by administration of male hormone, in both normal and anephric humans. Nevertheless, the process by which these hormones improve erythropoiesis is still controversial. Some of the highest levels of erythropoietin are observed in aplastic anemia.[69] Since the level is already supranormal in these patients, who are known to respond to androgen therapy,[70] Gardner and Nathan[71] suggested that the compounds act by evoking a proliferation of erythroid precursors that is independent of erythropoietin. Other investigators have studied the effects of testosterone[72] and androgenic metabolites[73] on in vitro cultures of human bone marrow and noted enhanced erythropoiesis. This suggests that the erythropoietic effect of androgens is independent of erythropoietin, since it is assumed that there is little or no erythropoietin in the marrow culture. Necheles[74] reported that erythropoietin and androgens together stimulated erythropoiesis in bone-marrow cultures more effectively than did either agent alone. Conceivably erythropoietin stimulates an erythropoietin-responsive cell in the bone marrow to differentiate into the erythroid line, and androgens are capable of causing the premature stem cell to differentiate into the erythropoietin-responsive cell.[67]

It is obvious that considerable controversy exists about the exact mode of action of androgens in the hypoproliferative anemia of renal failure. There is little doubt about their therapeutic efficacy, even in the anephric patient; and androgens have currently a firm place in our therapeutic armamentarium.

Combined Therapy and Its Results

At the Mayo Clinic, a pragmatic treatment for anemia of renal failure has been used for many years. It combines avoidance of excessive blood loss with supplemental administration of iron and vitamins, and use of anabolic steroids in addition to optimal hemodialysis.

Most of our patients are dialyzed three times weekly over periods of six to eight hours with capillary dialyzers (Cordis-Dow No. 4). Great care is given to rinsing the equipment adequately and assuring maximal blood return to the patient at the end of each dialysis. The patient is instructed to supplement his diet with vitamin A 4,000 units, ergocalciferol (D_2) 400 units, ascorbic acid 50 mg, thiamin mononitrate (B_1) 3 mg, riboflavin 3 mg, pyridoxine 3 mg, cyanocabalamin (B_{12}) 5 μg, nicotinamide 10 mg, folic acid 2 mg, and ferrous sulfate 150 mg. Serum iron and iron-binding capacity are determined twice per year and additional ferrous sulfate is given when the iron saturation is below 15% or the serum iron below 50 μg/dl.

Several anabolic preparations have been used without significant adverse effects. Mild alopecia, acne, and minor alterations in liver function are often seen. At present most of our patients receive either testosterone propionate (100 to 300 mg per week, intramuscularly) or fluoxymesterone (10 to 50 mg daily, orally).

Over the past 30 months hemodialysis has been performed approximately 7,000 times in 100 patients. During this time only 12 patients have required transfusion (28 units of leukocyte-poor blood) while receiving dialysis regularly. Only two patients required blood transfusions during the past year. In the 10-year history of the artificial-kidney center at the Mayo Clinic more than 200 patients have undergone chronic intermittent hemodialysis, but only two developed hepatitis while under our care. One of these received blood transfusions at an affiliated hospital from a different blood bank. The low incidence of hepatitis in this unit is probably a result of careful screening of blood donors and avoidance of blood transfusions.

Summary and Conclusions

Anemia of renal failure results from a complex process with features of blood loss, hemolysis and iron, and vitamin deficiencies as well as marrow hypoproliferation. Although erythropoietin activity is generally diminished (especially in the anephric patient), it rarely is absent; and there are data indicating the potential for a physiologic erythropoietic response to strong stimuli, such as hypoxia. Renal failure increases intra-erythrocytic levels of organic phosphates (particularly 2,3 DPG), which enhance dissociation of oxygen from hemoglobin in tissues where the oxygen pressure is low. Thus adequate oxygen is supplied to the tissue in spite of anemia. It has been suggested that this mechanism suppresses erythropoietic stimulation which otherwise would occur at similar levels of anemia.

Although adaptive mechanisms in the red bloo cell provide for adequate oxygen supply to th tissues, and so help to reduce subjective symptom of anemia despite very low hemoglobin levels this adaptation is precarious. Even rather smal blood losses may precipitate angina, hypotension, or other signs of circulatory compromise Improved red-cell production remains an important goal in the treatment of renal failure, and i can be achieved by optimal dialysis, provision o iron and vitamin supplements, and judicious us of anabolic steroids. Thereby it is possible to reduce transfusion requirements to a minimum an avoid the transfusion-related complications o hepatitis and sensitization to subsequent rena allografts. It should also be possible to permit th patient to donate blood for later autotransfusion For this purpose, red cells are separated fron plasma and leukocytes, washed, and then freeze dried for long-term storage. The immunologi advantages of such blood-banking are obvious.

Acknowledgment

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18-75. Will be found on page 424.

Chronic Primary Glomerulopathy

A Design for Study of Diagnosis and Treatment

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Today, the clinical approach to patients with glomerulonephritis should be by prospective study. The objective of such study would be to establish clinical, immunologic and renal functional characteristics that distinguish among broadly classified histologic subdivisions of glomerulopathy that may progress to end-stage renal failure. Although no drug regimen currently available has proven to benefit many patients with glomerulonephritis, one could employ controlled treatment trials in cases where the impairment of renal function is progressive. Ideally, such a study would be made on a cooperative basis and the design could serve for prospective, controlled studies of chronic primary glomerulopathy for now and in the future.

FOR 25 YEARS, attempts have been made with various therapeutic agents to influence glomerulonephritis. Beginning with nitrogen mustard, through adrenocorticosteroids, to combinations of steroids and cytotoxic, anticoagulant, and antiplatelet agents—drug upon drug has been tried. After this long effort it is disheartening that no drug regimen has been shown to influence ultimate renal function favorably. A basic reason for this lack of progress has been lack of rigor and thoroughness.

These qualities are necessary in the basic elements of such an investigation: (1) uniform criteria of morphologic diagnosis, (2) clinicopathologic correlations, (3) controlled therapeutic trials, and (4) long-term follow-up to determine prognosis. Additionally, we must accept the fact that the cause and origin of glomerulonephritis remain largely unknown. The deficient elements of morphologic diagnosis, clinicopathologic correlations that include controlled therapeutic trials, and long-term follow-up to determine ultimate outcome can and should be provided immediately.

These deficiencies have greatly hampered interpretation of the results of so-called treatment studies. To date, only four controlled therapeutic studies of chronic, primary glomerulopathy have been reported.

Controlled Studies of Treatment Reported

The Table lists the reports of controlled treatment studies according to drug used, type of glomerular lesion identified, number of patients in the study, follow-up period, and results. The two studies containing the largest number of patients are from Great Britain.[1,2] In the first,[1]

TABLE
Controlled Studies of Treatment for Primary Glomerulonephritis

Drug	Glomerulopathy	No. of patients Control	No. of patients Drug	Follow-up, months	Results, drug vs. control
Prednisone[1]	Minimal; membranous; proliferative	61	64	24	NS*
Prednisone and azathioprine[2]	Membranous; proliferative	77	72	6	NS†
Azathioprine[3]	Proliferative	14	5	9-16	NS†
Cyclophosphamide[3]	Proliferative	14	9	1-15	NS†
Heparin[4]	Proliferative	8	10	12	Drug better

*Not significant except in cases of minimal glomerulonephritis.
†Not significant.

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prednisone had no effect on the function of kidneys with membranous and proliferative lesions. The death rate was higher in the prednisone-treated group than in the control group. In patients with minimal glomerulonephritis, prednisone reduced proteinuria to a statistically significant extent. This investigation can be criticized because the dosage and duration of prednisone therapy varied greatly and patients with varied degrees of renal failure were accepted into the study. The inclusion of patients with irreversible glomerular scarring minimizes the chance of any improvement with steroid treatment and increases the likelihood of complications of this therapy. In spite of these objections, the conclusion that prednisone therapy is effective only in patients with minimal glomerulonephritis is accepted by most authorities.

In the second study,[2] patients with mostly membranous or mostly proliferative changes were admitted to a controlled trial of a regimen that combined azathioprine (2.5 mg/kg/day) with prednisone (20 mg/day for adults, 0.5 mg/kg/day for children). Patients with minimal glomerular changes were excluded. The control group was not given immunosuppressive drugs of any type. The treated group as a whole showed no evidence of benefit, and their mortality was higher. It can be concluded that the combination of these drugs in the doses employed and for the duration given offers nothing other than adverse complications to patients with chronic membranous and proliferative glomerulonephritis.

In a study of patients with intracapillary and extracapillary proliferative lesions,[3] a small group were given azathioprine or cyclophosphamide and compared with a small group who received no immunosuppressive drugs. During various short-term follow-up periods, neither group had any significant change in the serum creatinine, 24-hour urinary excretion of protein, or microscopic appearance of the lesions.

In a trial of heparin,[4] renal function improved significantly in eight of 10 patients treated with that drug and decreased progressively in six of eight control patients. Although the subjects were said to have chronic proliferative glomerulonephritis, the description of the criteria used in histologic diagnosis was not clear. Also, though the extremely low incidence of bleeding complications during heparin treatment raises a question as to what level of anticoagulation was achieved, no mention was made of clotting times.

An Approach to the Problem

In a prospective study, a basic approach to chronic, primary glomerulopathy can be made by classifying cases according to their histopathology and renal function. Within the initial broad histologic groups, immunologic assessment may identify subgroups. Patients in whom progressive renal disease is demonstrated may be treated with any reasonable drug regimen, so long as it is controlled.

Histologic Subdivision

Cases of glomerulonephritis without known cause may be classified morphologically for assignment to treatment groups. In making that assessment, one must recognize that morphologic changes are not separate diseases, but rather expressions which, in each case, most probably result from various stimuli. Even known systemic diseases, themselves different, can produce certain renal lesions that are quite similar morphologically: indeed, a specific etiologic diagnosis cannot be made in some cases without the clinical information.

One could define three broad categories of primary glomerulopathy: membranoproliferative, diffuse proliferative, and focal glomerulonephritis. Although it is possible to subdivide some of the groups, and that may become desirable later, entry into random-treatment groups could be determined by these three categories. Membranoproliferative glomerulonephritis, perhaps the largest group within this arbitrary classification, has many forms—including the well-known low-complement disorder[5] and the well-developed lesions of chronic lobular glomerulonephritis.[6] Glomerular obsolescence can occur in diffuse membranoproliferative disease by a more extensive accumulation of mesangial matrix that causes capillary collapse and subsequent hyalinization From the diffuse proliferative category,[7,8] poststreptococcal glomerulonephritis should be excluded, since most cases are self-limited and the small number that progress or recur have proved to be unaffected by any therapeutic agent. Focal glomerulonephritis should include both the proliferative and sclerosing forms of this chronic glomerulopathy.[9,10] Focal sclerosing glomerulonephritis may be difficult to diagnose initially, and its outcome is unfavorable in many cases.[10] Focal proliferative glomerulonephritis may be a progressive renal disease in some cases, especially those with heavy proteinuria when first seen.

Renal-Function Subdivision

Renal function, as determined by clearance techniques, may be normal or impaired when the patient is first examined. One could decide arbitrarily to place into various treatment groups only those patients with clear-cut evidence of progressive renal disease. A precise evaluation of renal function would be indispensable to this design. The judgment as to success or failure of a given drug regimen should depend to a large extent on the glomerular filtration rate. The tests that are most accurate require clearance determinations using constant infusion techniques (e.g., inulin clearance). Biologic and analytical variations should yield a standard deviation in inulin clearance of about 10%.[11]

So patients in a prospective study of glomerulonephritis could be classified according to their normal or reduced renal function. An arbitrary inulin clearance of 80 ml/min could separate normal from reduced renal function.

The Figure shows how inulin clearance might be used to determine improvement, stability, or a worsening of renal function after treatment. A 25% variation (clearly outside the range of analytic and biologic variability) could be used as proof of change of renal function in a given treatment group. Levels of proteinuria also, especially in those cases where protein loss initially was heavy, could be categorized as improved, stable, or worse in accord with arbitrary standards for excretion rates. Changes in proteinuria are obviously less important than changes in renal function in determining the long-term outcome of a given case.

Immune Mechanisms as Related to Glomerular Disease

In a prospective study of primary glomerulonephritis one should investigate the patients' capacity for immunologic reactivity in both humoral and cellular modalities to a variety of antigens of possible etiologic significance. Such investigations also could determine the usefulness of the reactions as diagnostic or prognostic indicators when patients entered the study.

The morphologic resemblance of some human glomerulopathy to experimental serum sickness and the presence of both immunoglobulins and complement along the glomerular basement membrane have led to the belief that in many such cases the deposition of antigen-antibody complexes in the kidney is the direct cause of injury.[12] The serum, urine, and tissue of patients should be examined for evidence of immune-complex deposition. In this way, one could perhaps further subdivide the groups of patients into immunologic and non-immunologic categories. Demonstration of immunoreactants in the glomeruli by immunofluorescence is of course the most convenient indicator of immunologic dam-

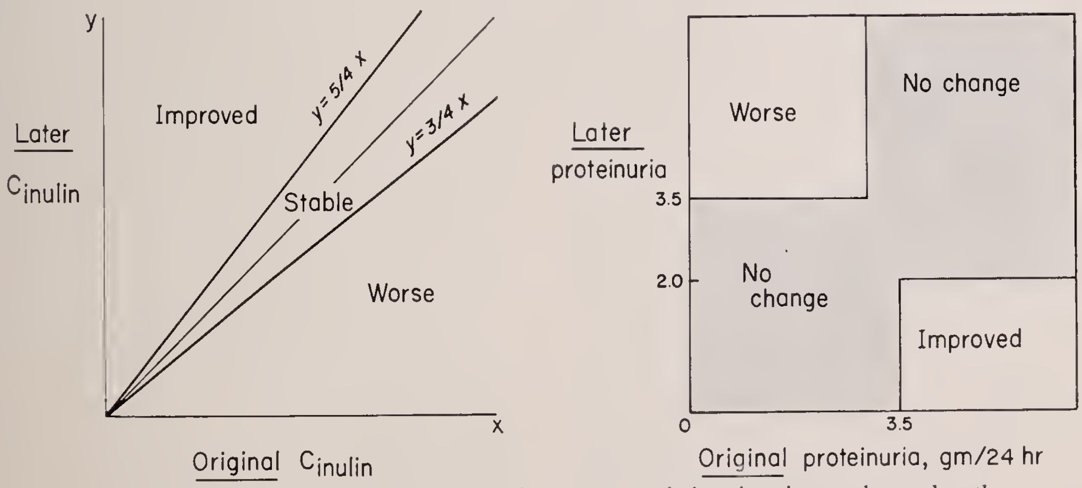

Figure.—Renal-function criteria for measuring outcome of chronic primary glomerulopathy.

age; but it is not absolute, because immunoglobulins have been found in the renal vessels and glomeruli of patients with diabetic and hypertensive nephropathy.[13,14] The presence of high- molecular-weight IgG in the serum and urine of patients with glomerular disease would provide firmer evidence that immune complexes in the circulation may be deposited in the kidney. Testing of sera, both with a monoclonal rheumatoid factor capable of precipitating immune complexes[15] and by precipitation with Clq.[16] may disclose immune complexes. The presence of complement-fixing activity in serum or body fluids is another sign of the probable presence of immune aggregates.[17]

Since the sera of some patients with glomerulonephritis are able to inactivate C3 by a mechanism that appears to be independent of the immune-complex mechanism.[18] the nature of any complement-fixing or anticomplementary effect in biologic fluids should be defined as carefully as possible in order to determine whether it represents an immunoglobulin complex. It has been established recently that an alternate pathway of complement activation exists. one that can bypass the fixation of C1, C2, and C4 and can be triggered by such substances as inulin, zymosan, properdin, and endotoxin.[19] Antibody probably is not essential for the activation of this mechanism.

The etiologic or functional role of cellular immunity under thymic regulation in glomerular disease is poorly understood. The findings of cellular-immune reactivity in patients with glomerular disease and the relationship of kidney antigen to glomerular disease are in conflict. One group[20] has not been able to corroborate the observation by another[21] that glomerular basement membrane is a putative autoantigen in a cell-mediated response in patients with glomerulonephritis. There is some direct evidence to suggest that viruses[22] and streptococci[23] may induce a cell-mediated immune response in glomerular disease. Organisms of the latter kind, of course, have been well identified by many as a causal factor in glomerulonephritis. Lymphocyte blastogenesis[24] and macrophage migration[25] could be the principal methods employed to investigate cellular immunity. Nonspecific mitogens measuring B and T cell regulated functional capacity of each patient's lymphocytes provide an internal control relative to the patient's capacity to respond. Glomerular and tubular basement membrane [26] and various viral and several streptococcal antigenic preparations also could be used in a screening panel in both cellular tests.

Treatment

Today, the least satisfactory element in the prospective study of patients with primary glomerulonephritis is treatment. No treatment currently available attracts enthusiasm for its potential benefit to such patients. So long as the patient can be made to understand this, treatment regimens may be employed under controlled conditions.

1. The treatment perhaps most important of all should be what may be termed *standard*. This encompasses attention to the patient's general health, extracellular fluid volume, blood pressure, and dietary intake of protein, calories, and sodium.

2. Because of the one controlled study that showed improvement,[4] an anticoagulant regimen may be justified. In addition, the Melbourne group has published several provocative papers concerning treatment with *anticoagulant and antiplatelet drugs*.[27-29] Such treatment is based on experimental and clinical data that prove an association between intravascular coagulation and progressive renal disease. Reports to date suggest that the following anticoagulant and antiplatelet drug regimens have been or may be used in humans: heparin alone; heparin and an antiplatelet drug (dipyridamole, aspirin, or sulfinpyrazone); heparin and an antiplatelet drug with later long-term warfarin treatment when heparin is stopped; and warfarin and an antiplatelet drug. Because of the ease of administration and follow-up, warfarin might be given to the outpatient and heparin to the more severely ill hospitalized patient. Presently, there is no definite answer to the question of which antiplatelet drug would be most suitable for patients with glomerulonephritis. Because aspirin inhibits the entire platelet release reaction at levels easily achieved by ingesting two to four 300-mg tablets per day, the drug action and cost favor this drug.[30]

3. Of the *cytotoxic agents*, studies to date suggest that cyclophosphamide—a potent antitumor agent of the alkylating drug group—is more promising than azathioprine. Cyclophosphamide has been used most extensively and effectively in the treatment for nephrotic syndrome in chil-

dren with minimal glomerular abnormalities.[31,32] Sustained remissions of the nephrotic syndrome ollowing cyclophosphamide treatment have been observed by several groups.[31,32] Its effectiveness in adults with mostly proliferative glomerulonephritis has not been shown, as indicated by the small study listed in the Table.[3] Also, in several uncontrolled studies it failed to produce significant improvement in renal function or protein excretion, or in various renal lesions, as evaluated from histologic comparison.[3,33,34] There are also major toxic manifestations, especially in the genitourinary system. Recently, irreversible sterility in males and females has been reported.[35,36] The potential benefit and risk for each patient should be assessed in the light of information as it becomes available. Severe and progressive glomerular disease, such as would be included in the study proposed, may endanger the patient so much that the potential hazards of cyclophosphamide would be relatively less significant. Short periods of treatment with cyclophosphamide—six months for example—could be proposed with sufficient precautions in a dosage range that should minimize occurrence of these complications.

4. A fourth treatment regimen could combine the *anticoagulant and antiplatelet regimen with cyclophosphamide*. The Melbourne group[29] found histologic improvement in patients with diffuse proliferative and membranoproliferative glomerulonephritis after treatment with a combination of such drugs, but no controlled study using this regimen has been reported.

Follow-up

In any such study, emphasis should be placed on long-term follow-up after the treatment period to determine ultimate renal function in the patient groups.

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31-36. Will be found on page 412.

Summary of the Rural Physician Associate Program Report to the State Medical Association House of Delegates on May 23, 1973

Prepared by John E. Verby, M.D., Director of the RPAP. Read by Joseph P. Connolly, M.D., Co-Director of the RPAP.

The Rural Physician Associate Program is sponsored by the Medical School, supported by the state legislative body, and implemented by the Department of Family Practice at the University of Minnesota. The Program began in September, 1971, with practicing physicians in the rural areas of the state volunteering as preceptors for one year to 25 medical students who had completed two years of undergraduate medical training. During their year's experience, these students were exposed to common illnesses in patients much more frequently than their peers who elected to remain in Medical School. They were able to follow the course of an illness from diagnosis through treatment to its eventual resolution and acquired confidence in diagnostic and mechanical skills. They developed an understanding in the roles of other health professionals and the community resources open to them and their patients for better health and disease care support.

In the traditional medical school setting, there is little or no contact with family practitioners. As the Medical School is now structured, students acquire knowledge from a large number of specialists, with no appreciation of the content of Family Practice nor attraction to its practice. Physician associates learned that approximately 80% of patient problems can be appropriately managed by a physician adequately trained in the knowledge and skills of Family Practice. They were able to see their therapeutic successes and failures in a more realistic manner and became comfortable in delivering care to a specific population. Many of these students will return to practice in a similar setting.

National Board scores of physician associate students compared favorably with the scores of classmates who remained in Health Sciences. Of the 23 students who completed the first year of the program, 12 are now tracking in family practice, six in medicine, two in pediatrics, two in psychiatry, and one in surgery. The overall cost of implementing, organizing, and developing the Rural Physician Associate Program is approximately $8,000 per student a year, including the $5,000 stipend provided by the taxpayers of the state but excluding the $5,000 paid by the preceptor physicians for student services.

Robert Baker

Robert Baker has been named associate director for operations at University Hospitals.

The appointment by *John Westerman,* general director of University Hospitals, marks the consolidation of operational responsibilities in one person.

Thomas Jones, Hospitals associate director, will continue to have primary responsibility for physical and programmatic planning. *Donald Van Hulzen,* Hospitals senior associate director, will be working with a special staff and department head task force to update the budgeting process.

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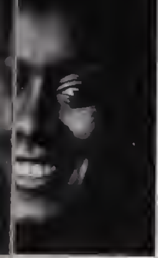

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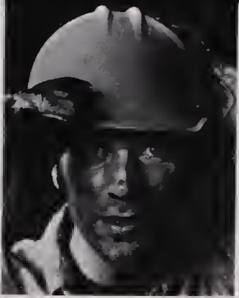

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The patient
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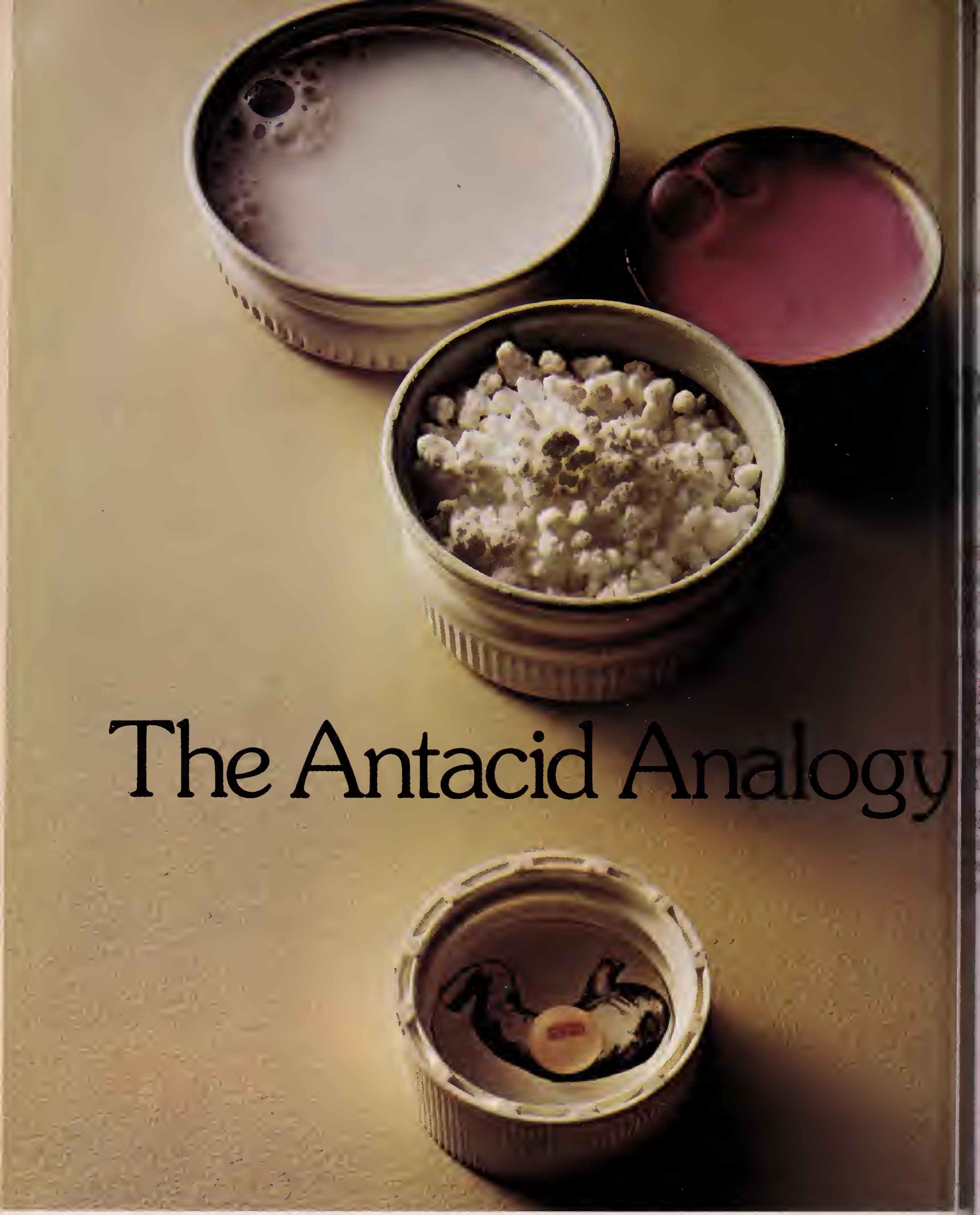

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*Innes, I. R., and Nickerson, M., in Goodman, L. S., and Gilman, A. (editors): The Pharmacological Basis of Therapeutics, ed. 4, New York, The Macmillan Company, 1970, p. 537.

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Editorials

Recent Advances in Nephrology

THE NEPHROLOGIST FINDS himself in close day-o-day contact with other physicians sharing comon interest in patients with problems of fluid nd electrolyte balance, renal lithiasis, hematologic nd neurologic complications of renal disease, diaetes mellitus, infections of the urinary tract, hyertensive disease and problems associated with ialysis and transplantation.

The spectrum of co-authors of the papers in this ephrology Issue reflects this multidisciplinary aproach to solving nephrologic problems. In addion to a resident and consultants from the Divion of Nephrology, the authors include several rologists, a transplantation surgeon, and an enocrinologist.

In assembling this issue no attempt has been ade to cover even the major areas of nephrology. his is rather a "sampler" illustrative of some of e interesting developments in the field. Major ncerns of nephrology, hypertension and hemoalysis have been omitted; hypertension has been nitted because a parallel special issue of this urnal is in the planning stages and dialysis has en omitted because that subject, and especially e impact of new federal legislation on this branch of nephrologic practice, will be dealt with in papers forthcoming from the Artificial Kidney Center of this Institution.

We offer these papers on renal transplantation (and particularly transplantation as treatment for the patient with renal failure due to diabetic nephropathy), the conservative management of chronic renal failure, anemia of chronic renal failure, and recent developments in lower urinary tract infection and renal lithiasis disease in the hope that this information will help your patients. The paper on chronic primary glomerulopathy[*] offers a rational approach to the cooperative study of these renal diseases for which, to date, no drug program has been proven to be beneficial.

Patients with renal disease have reason to expect increasingly more favorable results from treatment. Many factors are responsible for this improved outlook; the most important of these is increased cooperation between primary physicians and physicians working in tertiary care medical centers. We hope this partnership will be enhanced through personal communication and the printed word.

Cameron G. Strong, M.D.[†]
Guest Editor

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[*] See page 379.

[†] Chairman, Division of Nephrology and Internal Medicine, ayo Clinic and Mayo Foundation.

Renal Lithiasis

THE SUBJECT OF KIDNEY stones has been well covered in the literature and its importance can never be overemphasized. Each year approximately 1 in every 1000 inhabitants of the United States requires hospitalization because of kidney stones[1] and in a survey of 25,000 autopsies the incidence of kidney stones was 1.12 percent.[2] Unfortunately, in spite of extensive investigative efforts the etiology of stone formation in the majority of patients still remains a mystery.

Stone pathogenesis can be conveniently considered under two general headings: (A) factors resulting in an increased urinary concentration of stone crystalloids and (B) physiochemical changes in the urine conducive to stone formation at normal concentration of crystalloids.

The first category has been studied quite extensively. In this issue Wilson and others* have pointed out the importance, extent, and means of investigating calcium, oxalate, cystine, uric acid, and xanthine in patients with stone disease.

When the diagnostic evaluation is complete, usually no abnormality in crystalloid metabolism can be found and it then becomes apparent that factors relating to category (B) are at play. Assuming there are no obvious pH changes in the urine conducive to stone formation, and that stas or the presence of foreign bodies are not a fa tor, then it becomes evident that there is an al normality in one of the known or unknown pr tective factors which controls crystallization i the urine. Such factors are known to exist fro the simple empiricism that crystalloids present stones cannot be dissolved in water at concentr tions normally found in urine.[3] Wilson and othe point out that urinary citrate, magnesium, ar pyrophosphate are already known to inhibit stor formation and perhaps form the basis for tl empiric treatment of idiopathic stone disea with magnesium oxide and neutral phosphate A search for other inhibitory factors forms tl basis for much of the present-day research stone disease.

It is interesting that stone disease sits at tl interface of two disciplines. In the past one co cerned itself only with the immediate anatom needs of the patient while the other isolated its to pathophysiology. However, this is not true modern times. Wilson and others have show that by joining efforts, both the urologist ar the nephrologist can effect a uniform attack the problem of nephrolithiasis, for it is not un pathogenesis is better understood that treatme will be more effective.

William C. DeWolf, M.I
Minneapolis, Minnes

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*See page 368.

†Instructor, Department of Urology, University of Minnesota Health Sciences, Minneapolis, Minnesota.

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Renal Lithiasis

IN THE CURRENT article, Renal Lithiasis, An Optimistic Outlook, by Wilson et al.* of the Mayo Clinic, the authors present their logical approach to solving one of mankind's oldest known diseases.

Through the efforts of urologists and nephrologists working together, a better understanding of the multiple factors involved in so-called idiopathic metabolic stones is giving us a more optimistic outlook in management. They have gone f beyond the simple standard advice of drinki more fluids and restricting dairy foods. Even those cases of metabolically active stones, th report cessation of further stone formation in percent of patients. Nevertheless, the proble remain a challenge for further basic and clini research which is being pursued.

Gordon W. Strom, M
Minneapolis, Minnes

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*See page 368.

Recent Developments in Lower Urinary-Tract Infection

According to recent estimates, there were over 200,000 visits to primary physicians for cystitis and prostatitis last year in the United States. Therefore, it is appropriate that any issue of Minnesota Medicine dedicated to diseases of the urinary tract should include a discussion of the very important clinical problems of acute and chronic infections of the urinary tract. The paper by Segura and Smith* provides an excellent resume of the management of these problems and the paper should be required reading for family physicians.

In addition to the many important points stressed by the authors, I would like to emphasize that, not only should the practicing physician think in terms of controlling such infections, but also he should attempt to uncover significant underlying structural abnormalities of the kidney, ureter and bladder which may predispose to recurrent infections. Far too often the urologic surgeon sees a patient with advanced vesicoureteral reflux and pyelonephritis who has had antibiotic treatment alone for repeated urinary tract infections. In such cases, if a voiding cystourethrogram or even an intravenous pyelogram alone had been obtained early in the clinical course, the radiographs might have suggested that consultation with a urologist was indicated. The results of recent long term followup studies have shown that either symptomatic urinary tract infection or asymptomatic but persistent bacteriuria both are conditions which deserve a thorough evaluation and careful followup. We believe that the old canard to the effect that patients should have several infections before they are evaluated more thoroughly needs to be re-examined.

One important practical point with respect to managing adult females with recurrent infection is that they deserve a careful pelvic examination to determine if they have urethral-hymeneal-septal fusion. In this condition, the urethral meatus is located in the hymen and, therefore, it is pulled into the introitus during intercourse. These patients tend to have recurrent infections which have their onset coincident with beginning sexual activity, probably secondary to 'seeding' of the urethra and bladder. If these patients do not respond to conservative therapy they may benefit from a simple urethral transposition operation that moves the urethra away from the introitus by interposing a mucosal bridge between the urethra and the vagina.

The authors quite properly pointed out that these are simple techniques available which will allow the family physician to do urine cultures inexpensively in his office. I have included references to the commercially-available culture kits which we have found to be satisfactory.[1-3]

Elwin E. Fraley, M.D.
Chairman, Department Urologic Surgery
University of Minnesota

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*See page 361.

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Your daughters, too, what loves of girls—
What heads for painters' easels!
Come here and kiss the infant, dears,—
(And give it p'rhaps the measles!)*

---

*Thomas Hood, "Domestic Asides; or, Truth in Parentheses." 11:5, 1839.

Chronic Renal Failure

When treating chronic renal failure, the physician must not overlook any opportunity to improve renal function. Conversely, he must do nothing that will impair it further. Potentially treatable (although not necessarily curable) forms of chronic renal disease to be searched for include obstructive uropathy, pyelonephritis, nephropathy of analgesic abuse, uric acid nephropathy, hypercalcemic nephropathy, renal tubular acidosis, renal vein thrombosis and some forms of glomerulonephritis such as that associated with systemic lupus erythematosus or Wegener's granulomatosis. Treatable conditions that diminish kidney function regardless of the primary renal disease include congestive heart failure, dehydration, systemic infections, electrolyte imbalance, and hypertension.

One must avoid the administration of inappropriately large doses of potentially nephrotoxic drugs such as the aminoglycoside antibiotics and the polymixins. If possible, catabolic or anti-anabolic compounds such as adrenocorticosteroids and the tetracyclines should not be used. One also must avoid hypotension, hypokalemia and hyponatremia from overzealous use of potent diuretics. As noted by Anderson,* sodium restriction is indicated only if extracellular fluid volume is expanded, resulting in hypertension, pulmonary congestion or peripheral edema. The administration of urographic contrast media to dehydrated azotemic patients with multiple myeloma or with diabetic nephropathy plus congestive heart failure[1] can produce oliguric renal failure.

Anderson's attempt to discuss a complex subject, the treatment of chronic renal failure, in a short dissertation has led to certain oversimplifications and omissions. I believe most nephrologists would disagree with his definition of renal failure. Since the time of Addis, it has been known that an elevated blood urea can result from ingestion of a high protein diet or increased protein catabolism despite normal renal function. Adequacy of renal function is determined by the clearance of a substance, not by its plasma level. Additional physical findings include the grey-brown cutaneous hyperpigmentation due to retention of certain lipochromes and carotenoids, the pallor of anemia, the friction rub of uremic pericarditis and foot-drop due to motor neuropathy. The latter two are indications to initiate hemodialysis.

Estimating creatinine clearance from the plasma creatinine concentration using the formulas given by Anderson is fine for an average-sized patient, but many patients with chronic uremia have less than average muscle mass. This causes the serum creatinine to be misleadingly low. No mention was made of treating the anemia of uremia. In some instances, folic acid[2] or testosterone may prove beneficial. Otherwise blood transfusions are the only treatment available but are not necessary unless the hemoglobin falls below 8 gm/100 ml. Patients with cardiopulmonary disease may require transfusions at a higher level of hemoglobin.

Except for the above few comments, this reviewer agrees fully with Anderson's approach to the patient with chronic renal failure.

Donald A. Duncan, M.D.
Minneapolis, Minnesota

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*See page 364.

References

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Transcutaneous Stimulation

It is interesting to see yet another application of transcutaneous stimulation as documented by Crue and Felsoory in the March issue.* Any neurosurgeon would agree that a pain-relieving procedure done for malignant disease in its terminal stages should carry with it low risk, avoid the need for general anesthesia and not be dependent upon wound healing. Those have been the principles which have led to percutaneous cordotomy and other percutaneous approaches for destructive operations done on the spinal cord or dorsal root by the radio/frequency technic. More preferable would be a non-invasive means of creating pain relief. There have been many applications of electrical stimulation to the skin following Melzack's and Wall's gate control theory, with stimulation of large fibers to dampen incoming painful impulses over the A delta and C fiber system. As each of us gains more experience with the non-invasive technics of transcutaneous stimulation we are all impressed by the relatively small but present group of people who are aided by it for a period of time. It is of little importance from the patient's standpoint whether this may be of a placebo effect or whether it really has the capability of dampening the small fiber input system. Any transcutaneous procedure for pain ablation has its merit in a limited number of cases and so it is worthy of a trial before more rigorous open technics of destructive nerve surgery are employed in pain states. As Crue mentions, more work needs to be done in the field to improve on an imperfect and theoretical method of helping patients suffering from chronic pain states. We are all impressed with the fact that there isn't any single facet of a patient's anatomy that can be attacked surgically to guarantee alleviation of pain. It is again treatment of the patient as a whole—psychiatrically, psychologically, medically and surgically—in an effort to try to find a combination of factors in each individual circumstance which together are of low risk and rob the patient of as little function as possible in exchange for pain relief which is desirable.

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*See page 204.

Burton M. Onofrio, M.D.
Department of Neurologic Surgery
Mayo Clinic

Localization of Substernal Parathyroid Adenomas

THE ARRANGEMENT OF the anatomic structures of the neck is so constant that it is a joy to dissect when there has been no previous disturbance or scarring. For this reason the localization and removal of parathyroid adenomas in most cases is not particularly difficult for a surgeon experienced in the head and neck region.

On the other hand once there has been disruption of the normal anatomy by infection or scarring, dissection takes on a new dimension, and the incidence of complication rises rapidly. This applies to re-exploration for missed parathyroid adenomas.

In addition localization of substernal adenomas prior to surgery gives the surgeon confidence to split the sternum when the adenoma cannot be reached by dissection under the manubrium.

If the neck has been previously undisturbed, pre-operative localization by venous catheterization and serum parathyroid hormone studies as described by Lindall and Wong* would seem to be unnecessary. However, if there has been prior dissection in the low neck and especially a prior unsuccessful search for an adenoma, this technique should prove to be a big help to the surgeon.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

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*Lindall, A.W. and Wong, E.T.: Localization of Substernal Parathyroid Adenomas by Venous Catheterization. Minnesota Med 57:87, 1974.

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Letters to the Editor

Dear Editor:

This is a comment on the unreferenced, undocumented, and patently erroneous and misleading statements in a recent MINNESOTA MEDICINE editorial.* "Some have estimated that 70-80% of patients admitted to hospitals within the next ten years will be admitted for complications or chronic disease associated with an inherited genetic disorder." The author should be challenged to give the source or list the specific causes of admission which he prognosticates for the future and the associated inherited genetic disorders he postulates. Then one might attempt to challenge the surely nonsense thesis that heredity will play the predominant role for causing or precipitating such likely causes of hospital admissions as childbirth, infection, violence and accident, myocardial infarction, peptic ulcer, alcoholism, etc., etc. Careless quotations and sourceless or ridiculous statistics hardly strengthen an otherwise useful concept.

Henry Blackburn, M.D.
Professor and Director
Laboratory of Physiological Hygiene
University of Minnesota

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*Warwick Warren: Heredity vs environment. Minnesota Med 56:965, 1973.

Dear Editor:

Referring to the letter of Dr. Henry Blackburn concerning documentation about the incidence of genetic disease in hospitals in the future, it is always dangerous to extrapolate from a present data base but extrapolations that I referred to were made by Dr. Joshua Lederberg, Professor and Chairman, Dept. of Genetics, Stanford Univ. Medical School, in a statement to the Labor HEW Subcommittee of the Committee on Appropriations of the House of Representatives, June 10, 1970. Dr. Lederberg states "Today, at least 25% of all hospital beds and of all institutional places for the handicapped in this country are occupied by persons suffering some degree of genetic disease and an estimated 2 out of every 1000 persons—not counting relatives of the genetically ill—spend full time caring for them. Some authorities expect the percentage of the nation's health burden attributable to genetic causes to *double* in the next five years and in some places to absorb as much as 90% of available health facilities and services in ten years."

Although I cannot find the "some authorities" referred to by Dr. Lederberg, I do have a reference for the current content of genetic diseases in pediatric hospitals. This is from a Conference on Genetic Disease Control dated December 5, 1970, Washington, D.C. edited by Dr. Arthur G. Steinberg with conference coordinator, Dr. John F. Herndon. In this report Dr. Charles R. Scriver states on page 23 "We found that 9.3 percent of the children admitted to a large children's hospital were there because they had diseases of clearly defined genetic content. We found another 18% of admissions were the result of congenital malformations. The combined total for disease of greater or lesser genetic content is in the vicinity of 30%."

Obviously the figure of 70 to 80 percent is an estimation of what may take place in the future if progress continues as it has in the suppression of viral and bacterial diseases allowing a continuing progressive increase in the incidence of direct genetic and genetic-related disease.

Thank you very much for the opportunity to bring again to the attention of the physicians in Minnesota the significant importance of genetic disease.

Warren J. Warwick, M.D.
Associate Professor
Department of Pediatrics
University of Minnesota

Letters to the Editor

Dear Editor:

The article "Fatal Mumps Myocarditis" in the April issue* described a patient with parotitis who died three days after onset. The author concluded that the myocarditis and parotitis were due to the mumps virus. It is my judgment that from the data presented, a diagnosis of mumps myocarditis is not justified.

Parotitis may be caused by a host of viruses. A recent report from the Cook County Hospital[1] has shown that parainfluenza 3 virus can be a cause of parotitis. To date, a partial list of viruses which can cause parotitis includes cytomegalovirus, parainfluenza 1 and 3, coxsakie, echo and choriomengitis viruses.[2] The essential serologic or other tests to determine the presence of the mumps virus were not done in this case. Myocarditis can also be caused by some of these viruses.

Because myocarditis, secondary to mumps, is rare[3,4] if existent at all, one must carefully document the etiologic agent when reporting such a rare occurrence. The few cases previously reported assumed that the cause of the parotitis was the mumps virus due to the inability at that time to identify the other viruses.

The interval between the onset of the myocarditis following the parotitis was of a much shorter interval then is usually expected, which makes the causal relationship between them suspect.

Julian L. Berman, M.D.†
Cook County Hospital
Chicago, Illinois

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*Page 285.
†Professor of Pediatrics.
Chairman, Department of Medical Education.

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2. Editors Commentary in Year Book of Pediatrics 1974: S. S. Gellis, ed. p. 78 Year Book Med. Publishers, Chicago 1974.
3. Bradford WL in Brennemann's Practice of Pediatrics Vol. II Chap. 13 p. 7, 1968.
4. Brown R, former Associate Chairman, Department of Pediatrics, Cook County Hospital: personal communication.

Dear Editor:

I concede the point made by Professor Berman. Serologic tests were not performed to identify the virus as the mumps virus. I was in fact, unaware that other viruses could cause parotitis According to the. point made by Professor Berman, unless serologic tests are performed, a certain number of cases clinically diagnosed as mumps are in fact, parotitis with a different viral etiology. It would seem that the case reported here could have been such an instance.

James C. Kussy, M.D.
Little Falls, Minnesota

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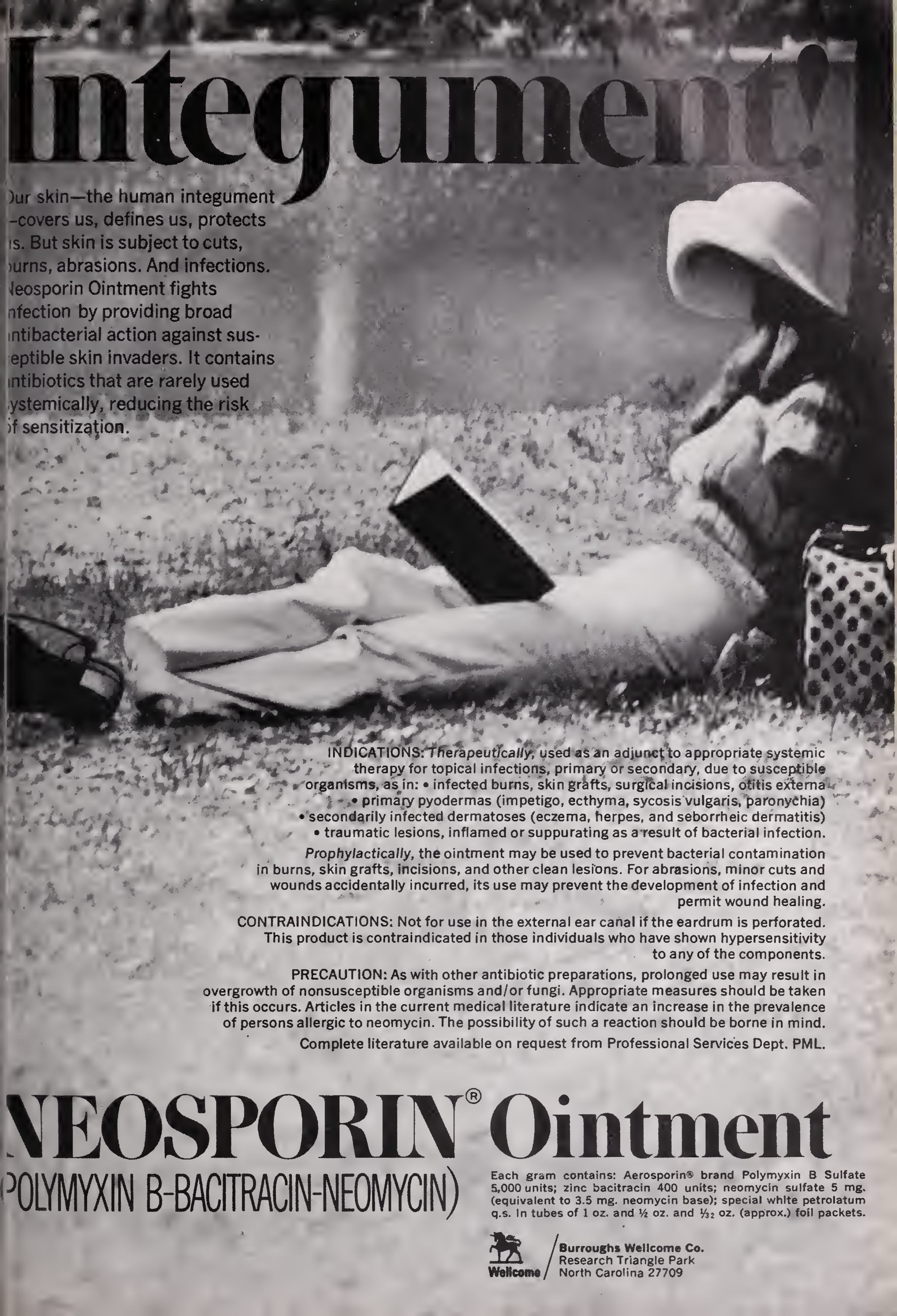

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eptible skin invaders. It contains
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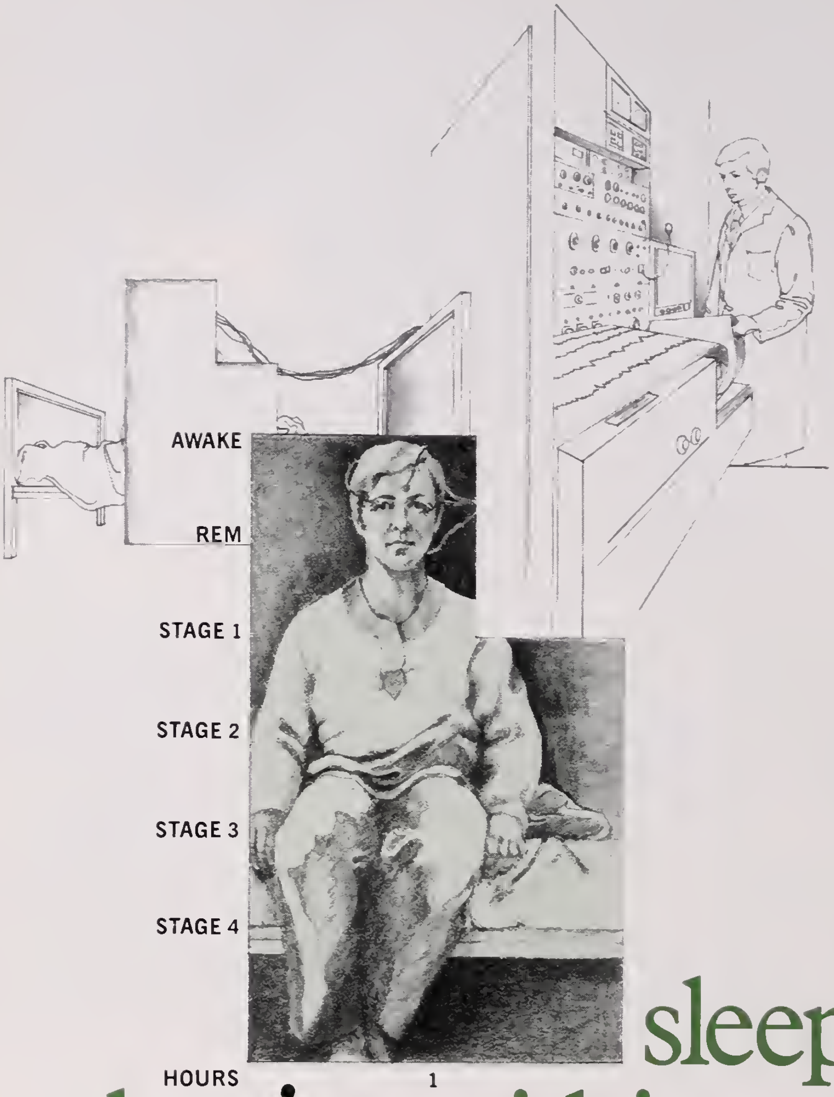

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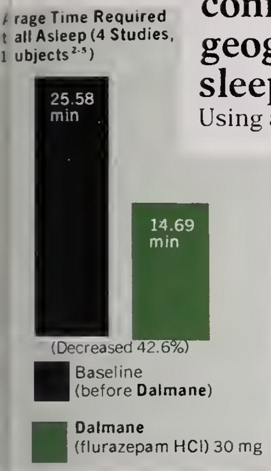

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:rse Reactions: Dizziness, drowsiness, lightheadedness, gering, ataxia and falling have occurred, particularly in elderly bilitated patients. Severe sedation, lethargy, disorientation and ı, probably indicative of drug intolerance or overdosage, have reported. Also reported were headache, heartburn, upset ach, nausea, vomiting, diarrhea, constipation, GI pain, nervous- talkativeness, apprehension, irritability, weakness, palpitations, t pains, body and joint pains and GU complaints. There have been rare occurrences of sweating, flushes, difficulty in focusing, ed vision, burning eyes, faintness, hypotension, shortness of th, pruritus, skin rash, dry mouth, bitter taste, excessive saliva- anorexia, euphoria, depression, slurred speech, confusion, ssness, hallucinations, and elevated SGOT, SGPT, total and t bilirubins and alkaline phosphatase. Paradoxical reactions, excitement, stimulation and hyperactivity, have also been rted in rare instances.

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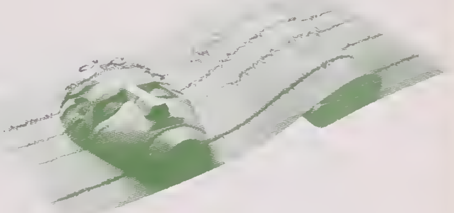

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Opinion & Dialogue

Is there a need for a drug compendium?

Government Health Official

Henry E. Simmons, M.D.
Deputy Assistant
Secretary for Health
Department of Health,
Education and Welfare

A drug compe
of the type I env
would fill a defini
need for the p
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compendium
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fashion.

What a Compendium Should Contain

I believe the compendi
should inform the doctor wh
drug will do, when he should
for what type of patient, for
long, in what dose, what ben
his patient is likely to obtain,
risks involved, and cross-rea
with other drugs.

The information would
based on the package insert
have the same legal status. I
a complete compendium wit
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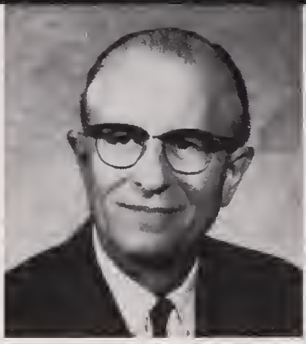
might even eliminate the ne

Maker of Medicine

Joseph F. Sadusk, Jr., M.D.
Warner-Lambert Company



A drug compendium,
preferably compendia, shou
believe, be private, not feder
sponsorship. They should co
comprehensive listings of dr
available for prescribing. Th
should be single, legibly prir
volumes of reasonable size,
dated quarterly or semiannu
and completely revised ever

Function of a Compendium

A compendium should
nish the following informatic
drugs in the following order:
tions for use, side effects, ac
drug reactions, contraindica
drug interactions, drug dosa
the dosage forms marketed.
prices should not be include
cause they vary so widely an
change rapidly.

No compendium shoul
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must be left for the practicir
sician to decide, whether on
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own clinical experience, adv
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by manufacturers, and so or

Nor should a compend
undertake to educate the do
how to use drugs. Rather, it
be a reference source desig
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drugs he may not use regula

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y a complete compendium,
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rmous amount of repetition.
, drugs should be arranged
s. Mutually applicable infor-
would be provided, along
ief discussions pinpointing
nces in specific drugs of
ass. Listings would be cross-
d in a useful way.

Available Documents as s of Information

xisting references such as
nd the AMA Drug Evaluation
viously useful but they are
olete. Either they are not
eferenced by generic name
not group drugs with simi-
racteristics, or they do not
the available and legally
ted drugs. And some of
omitted may be very useful.

On the other hand, drugs made by more than one supplier, tetracycline for example, may be fully described a dozen times in the same book.

While perhaps PDR could be rearranged and cross-indexed with generics included, and while the AMA Drug Evaluation might also be modified and expanded, I am not sure that the end result would have all the attributes required for a useful compendium. At the same time, you would run the risk of amassing a voluminous and unwieldy tome.

Should Editorial Comments Accompany the Listings?

Subjective judgments, in my opinion, have no place in a compendium. However, if there is substantial evidence based on a sound body of science concerning relative efficacy of several drugs, certainly that information should be included. The committee of experts compiling and editing a particular section would also have to assess and indicate instances where a meaningful difference between drugs is pertinent.

Sponsorship, Compilation and Editing

Producing a book like this would undoubtedly be difficult and demanding. It would obviously take a great deal of talent and expertise, and would require a varied and experienced group, ranging from writers and editors to highly skilled clinicians and pharmacologists. Style, format and clarity of language would play an important part in determining the usefulness of the book. And it should be updated periodically and completely revised annually.

I have no opinion whether the government or the private sector should sponsor and/or finance the compendium. What is most important is that the compendium be an authoritative, objective and useful source of information for the doctor to have at hand as a ready reference.

l in no way imply control over
actitioner's prerogatives.

nother Compendium?

practicable, single-volume
endium cannot, nor is it
sary to, include all drugs on
arket today. From my prac-
internal medicine for some
rs, my experience as a con-
t, and as a faculty member
or five medical schools, I
estimate that a doctor uses
0 to 35 drugs regularly. The
Physicians' Desk Reference,
ntally, contained about
entries.

s to whether there should be
ral compendium, in my opin-
stated earlier, the answer is
-there should *not* be one. The
sal assumes that existing
endia are inadequate. We're
re of that at all. Whatever its
fections, the present drug
ation system in the U.S. is
multifaceted, pluralistic and
sive. Good compendia exist,
l as other ample sources on
herapy, ranging from journal
ure through AMA Drug Evalu-
o company materials. Not
sicians may use such
es as often or as well as they
l, but that is the fault of the
not of the sources.

n any event, rather than produce another book, it makes much more sense to work on improving existing compendia, and perhaps they could, as knowledge advances, include more accumulated clinical data and experience, and more information on drug interactions and adverse reactions.

Implications of a Federal Compendium

Take a hard look at the implications of a federal compendium. It would have the force of law, virtually dictating what drugs to use and how to use them. In effect, it would be a regulatory document with legal or quasi-legal status, posing medical/legal problems similar to those the doctor may now encounter if and when he departs from the provisions of the package insert. A compendium under federal aegis would tend to restrict decisions on drug therapy to one orthodox level—a most dangerous trend for medicine.

New Compendium—A Medical Option

I detect no ground swell of initiative or support whatsoever for a federal compendium—or, for that matter, for a new compendium of any type. A 1969 PMA survey conducted by Opinion Research Corporation found that only 15 per cent of those physicians interviewed felt a new compendium was needed. And a large majority did not favor the involvement of the federal government if one were to be created, preferring instead a nongovernmental consortium.

Even if we come to a time when the medical profession itself opts for a new kind of compendium, it should be handled and financed, ideally, outside both government and industry. Final review and editorial authority could be delegated, say, to specialty bodies and medical societies—but above all, *not* the government.

Surely the health care system in the United States has far more vital matters to consider than the extensive cost and effort that would have to go into the preparation and maintenance of a new, monolithic compendium, and especially one bearing the imprimatur of the federal government.

Opinion & Dialogue

What is your opinion, doctor? We would welcome your comments.

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Painful Ribs

This patient is a male, 75-year-old who complains of pain in the ribs. Pain is exacerbated by straining or lifting.

In the past several weeks he has experienced a 20 lb. weight loss, anorexia, and fatigability.

There is marked tenderness to palpation of the rib cage.

Bone Scan (Figure 1): There are multiple abnormal concentrations of tracer material (99mTc.-pyrophosphate) in the ribs. The distribution of the tracer material in the remainder of the skeleton is normal.

X-Rays (Figures 2 and 3): Multiple, sharply demarcated, lytic defects are present throughout all bones. There are multiple fractures of the ribs. (arrows) There is an old healed fracture of the left clavicle.

What is your diagnosis? (See next page.)

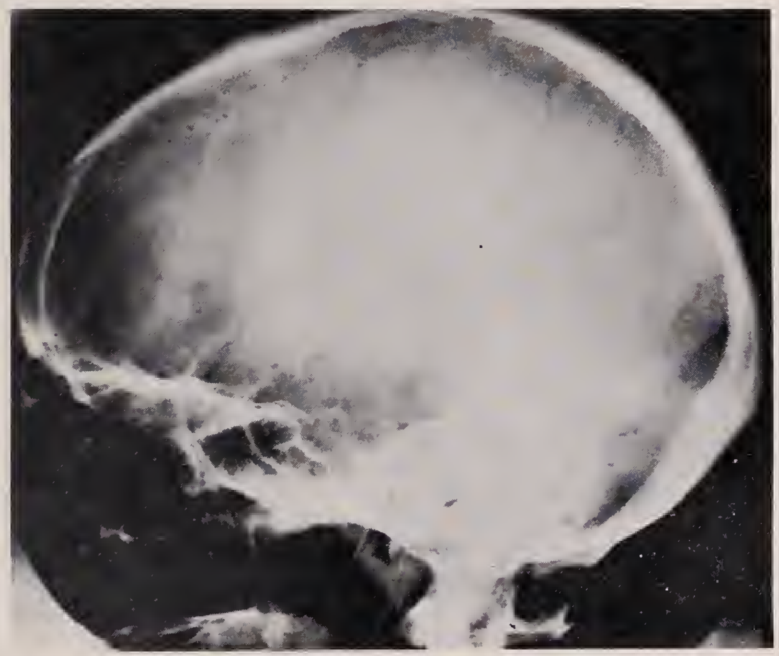

Figure 2

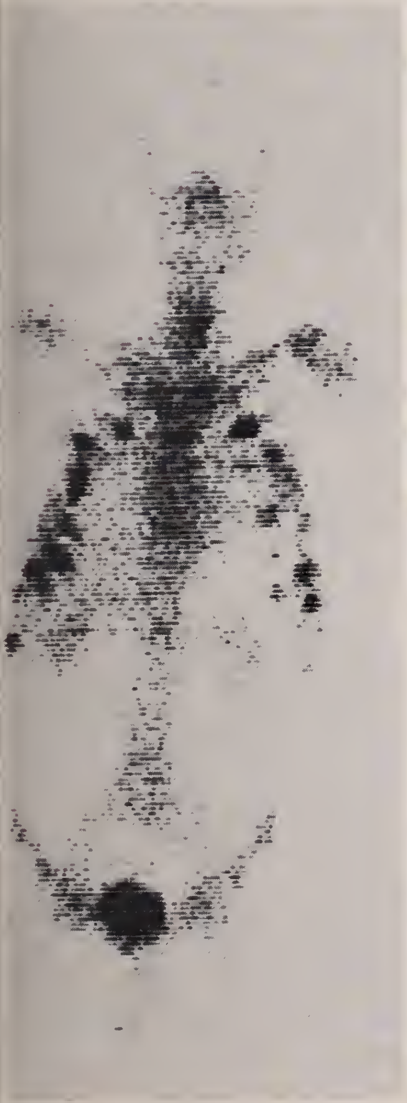

Figure 1

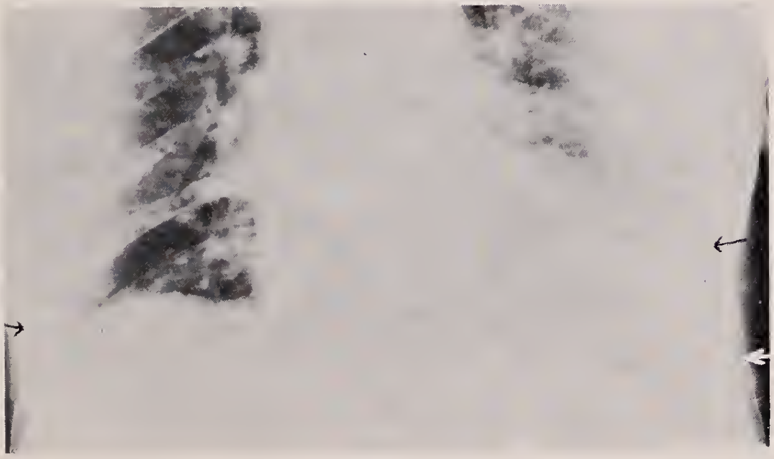

Figure 3

Diagnosis: Multiple rib fractures in presence of Multiple Myeloma.

Discussion

There are multiple defects distributed throughout the skeleton which have the sharply demarcated, lytic appearance associated with multiple myeloma.

Diagnosis was confirmed by bone marrow biopsy.

The scan is striking in that it is abnormal only in areas of fracture but does not demonstrate any abnormal uptake in the areas of bone destruction; nor is there any uptake in the old healed clavicular fracture.

Bone scanning has recently taken on new importance because of the advent of improved tracer materials and scanning equipment. Nevertheless it is important to be aware of the limitations of the bone scan. The formation of an abnormal scan depends on the deposition of tracer material in reactive new bone. Not all bone lesions will stimulate this reaction and myeloma is well known as one of these. In spite of the fact that the bone lesions of myeloma do not exhibit uptake of tracer material, bone scanning is helpful in evaluation of bone pain.

As demonstrated by Charkes et al.[1] bone pain in myeloma is usually related to fraction or infraction and not related to the presence of "punched out" foci of osteolysis per se. Scanning techniques are very helpful in demonstrating these areas.

Bone scanning in multiple myeloma is useful if the following points are kept in mind:[1]

1. The lytic defects of myeloma are not demonstrated on the bone scan.
2. Abnormal uptake is usually related to bone infraction.
3. Bone pain is usually related to infraction and not the lytic lesions.
4. Abnormal tracer uptake may precede roentgenographic changes by three to ten months.
5. A negative bone scan in multiple myeloma makes infraction unlikely, and other causes of pain should be sought.

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1. Charkes ND, Durant J and Barry WE: Bone pain in multiple myeloma. Arch Intern Med 130:53, 1972.

The Minnesota State Board of Medical Examiners

The Minnesota State Board of Medical Examiners wishes to express its appreciation to Minnesota State Medical Association who worked very hard for the successful passage of the bill which abolished the Basic Science requirement in Minnesota. Signed by Governor Wendell R. Anderson on March 23rd, the bill became effective March 25, 1974.

Passage of this bill enabled this Board to immediately license sixteen physicians who had passed the FLEX examination and met all the requirements for licensure in Minnesota.

Bror F. Pearson, M.D.
Secretary-Treasurer

The High Risk Newborn

Management and Outcome of Prematurity, Respiratory Distress Syndrome (RDS) and Other Major Neonatal Problems

CARL E. HUNT, M.D.*

Optimal care of the high risk newborn can contribute to reduced neonatal nortality rates and, most important, to improved quality survival. Achievement f optimal neonatal survival rates and developmental outcome requires attention o the following priorities: (1) Earlier recognition and improved management of he high risk pregnancy and delivery and optimal utilization of neonatal centers vith emergency transport capabilities; (2) Avoidance of cold stress; (3) Achievenent of adequate nutrition within the first two-three days of life and of optimal aloric and protein intake within the first week; (4) Maintenance of adequate ydration in the small premature; (5) Earlier recognition and therapeutic intervenion in all neonatal surgical abnormalities and (6) Earlier recognition of deteriorating respiratory status and provision for appropriate assisted ventilation prior to he actual occurrence of hypoxia.

An increasing number of high risk new-orns can now survive the neonatal period (first nonth of life). Evidence is gradually becoming vailable to confirm that improved quality survival (developmental outcome) can also be achieved.[1]

The Neonatal Intensive Care Unit (NICU) at Jniversity of Minnesota Hospitals began full opration in January, 1970. The purposes of this reort are to: (1) summarize outcome in the 1200 igh risk newborns admitted to the NICU in 1970-72, (2) relate outcome to the various potential roblems of the high risk newborn and (3) sumnarize currently available data regarding developnental potential in the survivors of neonatal inensive care.

Patient Population and Clinical Facilities

Approximately 95% of the NICU admissions vere born elsewhere and later transferred to Uniersity of Minnesota Hospitals, usually within the irst week of life and often (50%) within the first wo days. Transport was accomplished by ambuance for distances of less than 60-70 miles and by fixed wing aircraft for longer distances. For both ambulance and air transport, the transport team consists of a nurse and physician experienced in emergency neonatal transport.

The NICU can accommodate 20 critically-ill infants. A computer monitoring system is available and a fully equipped microchemistry laboratory is adjacent to the NICU. Physicians are in attendance 24 hours a day, seven days a week. The nurse/patient ratio ranges from 1:1 for the most critically-ill neonates to 1:3-4 for convalescing patients.

Results

The survival rates for 1970-72 are summarized in Table 1. During this three-year period the

TABLE 1

NICU Survival Rates at University of Minnesota Hospitals in 1970-72. Approximately 90% Were Less than One Week of Age When Admitted.

Outcome	1970	1971	1972	Total
Survived (%)	200 (66%)	266 (69%)	376 (74%)	842 (70%)
Died	102	120	134	356
Total	302	386	510	1198

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number of neonatal admissions increased from 302 to 510 and the survival rate increased from 66 to 74%. Survival statistics for the individual neonatal conditions are summarized in Table 2. As expected, prematurity and Respiratory Distress Syndrome (RDS) are the two most frequently encountered potential problems of the high risk ne born.

The number of premature newborns admitt increased from 130 in 1970 to 213 in 1972. T most significant increases in premature surviv rates occurred in the 1000-1499 and 2000-24

TABLE 2

Survival Rates for the Individual Neonatal Conditions in Neonates Admitted to the NICU at University of Minneso Hospitals in 1970-72. The Individual Groups Listed are not Mutually Exclusive. The Severe RDS Group Includes RDS Patients Requiring Intubation and Assisted Ventilation. The Group of Neonates with DIC Does Not Inclu Any Patients with DIC Only As A Terminal Event.

	1970		1971		1972		Total	
Diagnosis	Survival	Total	Survival	Total	Survival	Total	Survival	Total
Prematurity*:								
<1000	1 (9%)	11	2 (20%)	10	4 (17%)	23	7 (16%)	44
1000-1499	7 (28%)	25	17 (33%)	51	22 (47%)	47	46 (37%)	123
1500-1999	26 (61%)	43	29 (69%)	42	43 (61%)	70	98 (63%)	155
2000-2499	35 (69%)	51	48 (77%)	62	66 (90%)	73	149 (80%)	186
TOTAL	69 (53%)	130	96 (58%)	165	135 (63%)	213	300 (59%)	508
Respiratory Distress Syndrome:								
Mild: No assisted ventilation	29 (100%)	29	71 (94%)	76	57 (95%)	60	157 (95%)	165
Severe: assisted ventilation	9 (16%)	58	15 (21%)	73	47 (41%)	116	71 (29%)	247
TOTAL	38 (44%)	87	86 (58%)	149	104 (59%)	176	228 (55%)	412
Transient Tachypnea	8	8	12	12	20	20	40	40
Sepsis/Meningitis:								
—E. Coli	2	9	3	17	5	11	10 (27%)	37
—Pseudomonas	0	6	0	2	1	4	1 (8%)	12
—Klebsiella	2	6	2	10	2	11	6 (22%)	27
—Other	6	14	8	8	12	21	26 (60%)	43
TOTAL	10	35	13	37	20	47	43 (36%)	119
Infants of Diabetic Mothers	2	2	5	5	11	14	18 (86%)	21
Erythroblastosis Fetalis	5	7	8	10	6	9	19 (70%)	26
Necrotizing Enterocolitis	1	3	2	10	18 (53%)	34	21 (44%)	47
Surgical:								
T-E Fistula	5	7	5	6	3	3	13 (81%)	16
Gastroschisis & Omphalocele	2	2	4	5	4	5	10 (83%)	12
Intestinal Atresia	4	4	3	3	7	9	14 (88%)	16
Diaphragmatic Hernia	2	3	0	4	2	4	4 (36%)	11
Other	5	9	10	13	13	17	28 (72%)	39
TOTAL	18	25	22	31	29	38	69 (73%)	94
Congenital Cardiac								
—Coarctation	9	15	7	11	3	14	19 (47%)	40
—Complete Transposition	11	19	4	7	11	13	26 (67%)	39
—Hypoplastic left Heart Syndrome	0	10	0	13	0	7	0	30
—Other	12	17	20	32	19	26	51 (68%)	75
TOTAL	32 (52%)	61	31 (49%)	63	33 (55%)	60	96 (52%)	184
Disseminated Intravascular Coagulation (DIC)	2	17	1	23	4	44	7 (8%)	84

*Listed by birth weight range, in grams.

gram categories. Although survival in prematures with birth weights of less than 1000 grams has increased from 9% in 1970 to 17-20% in 1971-72, he actual number of survivors is still quite small.

The number of RDS admissions increased from 87 in 1970 to 176 in 1972. Approximately 10% of cases have occurred in full-term infants. Severity of RDS has been classified as mild or severe depending on the need for assisted ventilation. The high frequency of severe RDS (60%) is due to selection for referral of only the more critically-ill RDS newborns.

The indications for assisted ventilation were one or more of the following: (1) breathing 100% 0_2, an arterial $P0_2<40$ mm Hg at any age, less than 50-60 mm Hg if under 12 hours of age; (2) cyanosis while breathing 100% 0_2; (3) opacified lung fields by thoracic roentgenogram; or (4) apnea or slow, gasping respirations. Since May, 1971, positive end expiratory pressure (PEEP) has been utilized whenever adequate arterial oxygenation cannot be achieved with intermittent positive pressure breathing (IPPB) and inspired 0_2 levels of less than 30-40%.

The vast majority (95%) of RDS patients not requiring assisted ventilation have survived the neonatal period. The change in overall RDS survival between 1970 and 1972 is related entirely to the increase in severe RDS survival from 16% in 1970 to 41% in 1972. The potential for survival in severe RDS patients requiring assisted ventilation is also directly related to birth weight (Table 3). Although no patients under 1.0 Kg birth weight survived during this time period,* 68% of those with birth weights of at least 2000 grams have survived.

A total of 119 cases of sepsis/meningitis occurred in 1970-72 and only 36% survived. All neonatal admissions with a documented bacterial sepsis and/or meningitis anytime during the acute illness have been included in this group. Many of these occurrences were related more to postnatal events or problems than to prenatal considerations such as premature ruptured membranes. Isolated meningitis was extremely uncommon in this group of neonates. Survival rates were highest (60%) in gram positive sepsis and lowest (8%) in Pseudomonas sepsis. The potential for survival, especially quality survival, was best when there was a high index of suspicion for infection, with early recognition and early treatment prior to the onset of significant acidosis, shock, disseminated intravascular coagulation (DIC) or other evidence of clinical deterioration.

The majority of the infant of diabetic mother (IDM) patients (88%) survived their acute neonatal problems. Hypoglycemia, the major potential problem of the IDM, will be reflected not in survival rates but rather in the *quality* survival (developmental outcome) of these children.

The newborns with erythroblastosis fetalis all had severe hemolytic disease, with most of them requiring at least one exchange transfusion. Nineteen (70%) of the 26 patients survived; prematurity and its complications were the major problem in the seven nonsurvivors. The potential for survivial in these high risk newborns is optimal only if prenatal care is optimal, i.e. only if stillbirth or severe hydrops can be prevented by the judicious use of intrauterine transfusion(s).

A total of 47 cases of necrotizing enterocolitis (NEC) occurred in 1970-72. All but five patients were premature. In each of the five full term infants, significant perinatal asphyxia and/or subsequent hypoxia and acidosis had been present; only two of these five survived. Seventy-five percent of the 42 premature newborns had RDS with more severe RDS in the nonsurvivors. In the non-RDS prematures, significant perinatal asphyxia, shock, or hypoxemia from other causes occurred in approximately two-thirds of the group. Although overall survival was only 44%, 18 (53%) of 34 patients in 1972 survived. Of the total group, 68% demonstrated signs of peritonitis and/or perforation and required surgical intervention: 39% of those requiring surgery survived as com-

TABLE 3

Relationship of Birth Weight to Survival in RDS Newborns Requiring PEEP. These 154 Patients Represent All Those Requiring PEEP from Its Introduction in May, 1971 through March, 1973.

The Frequency of Pneumothorax Was Distributed Evenly among the Several Birth Weight Groups. During This Same Time Period, Pneumothorax also Occurred in 13 RDS Patients not Receiving Assisted Ventilation.

	Number of Patients		
Birthweight	Survived	Died	Total
<1000	0	9	9
1000-1499	5 (12%)	36	41
1500-1999	20 (38%)	32	52
2000-2499	21 (68%)	10	31
⩾2500	12 (57%)	9	21
TOTAL	58 (38%)	96	154
Associated Pneumothorax	15 (29%)	36	51

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*Thus far in 1973, two prematures under 1000 grams and requiring PEEP have survived.

pared to 62% survival in those who could be managed medically.

A total of 184 neonates with congenital heart disease were admitted to the NICU in 1970-72. Of this group, 96 (52%) survived. Of the 88 deaths in this group, only about 40 were related to inoperable cardiac disease, the majority of these being hypoplastic left heart syndrome. Most of the other deaths were secondary to clinical deterioration before appropriate diagnostic and therapeutic intervention could be achieved.

A total of 94 patients with noncardiac surgical problems were admitted to the NICU in 1970-72. Sixty-nine (73%) survived. Early diagnosis and surgical intervention, and appropriate postoperative management, have led to a greater than 80% survival in those with intestinal atresia, tracheo-esophageal fistula, omphalocele or gastroschisis. The poor survival rate in diaphragmatic hernia (36%) confirms our clinical impression that this entity requires very early surgical intervention, ideally within the first few hours of life.

Major Neonatal Problems

The various factors listed in Table 4 represent the major clinical situations and diagnostic categories which have affected outcome in patients admitted to our NICU. Although all the factors listed can obviously affect survival rates, the primary impact of these factors may well be on quality rather than quantity survival. The following comments represent a synthesis of conclusions based on currently available information in the literature and on our experience with the high risk newborns reported here.

Cold Stress

Hypothermia (cold stress) is a very frequent but totally preventable neonatal stress.[2,3] The newborn infant, and to an even greater extent the premature infant, has a disproportionately large body surface area (BSA) as compared to the olde child or adult. Subcutaneous fat, which acts both as insulation and as an energy source, decrease in amount as the degree of prematurity increases

TABLE 4
Major Clinical Situations and Diagnostic Categories which Affect Outcome in the High Risk Newborn. In Survivors, These Factors Can Have a Major Impact on Quality Survival.

1. Cold stress (hypothermia)
2. Nutrition
3. Hyperbilirubinemia
4. Prematurity
5. RDS
6. DIC
7. NEC
8. Surgical Conditions: Cardiac
   Noncardiac

The full-term infant ordinarily requires an ambient temperature of 92-95°F and the prematur newborn 96-100° during at least the first day o life. The increased BSA and prolonged exposur to a cold delivery room are adequate to provid a cold stress in any newborn infant. Because of hi decreased insulation and energy stores, however the premature infant requires an ambient temperature much closer to body temperature, is les tolerant of a brief cold stress, and is much mor likely to become hypothermic in response to cold stress.

The full-term or premature infant responds t a cold stress by increasing O_2 consumption in order to increase heat production. When energy reserves and/or adequate O_2 are no longer available the body temperature begins to fall, and progressive metabolic acidosis begins to develop. The end result of this chain of events leading to hypothermia is progressive and eventually irreversible metabolic acidosis. When hypothermia is allowed to persist, even an initially healthy newborn can be converted rather quickly into a critically-ill neonate who may not even be able to survive the cold stress, especially if superimposed on other neonatal problems. In fact, by inhibiting surfactant production, the severe acidosis occurring in response to hypothermia can convert a newborn with normal lungs into one with severe RDS. From a practical point of view, however, what occurs most frequently is that a premature infant with RDS is subjected to a cold stress, becomes hypothermic, develops acidosis, and ultimately developes a greater severity of RDS than would otherwise have occurred.

Nutrition

Depending on adequacy of the thermal environment, the newborn infant requires 120-150 cal/Kg/day for optimal growth. Optimal nutrition also requires adequate protein intake, the full-term infant requiring 2.0 and the premature 4.0 grams/Kg/day. Since active development of the central nervous system is still occurring in the newborn, and to a proportionately greater degree in the premature infant, malnutrition in the neonate can have devastating and permanent effects on developmental outcome (see discussion) even though survival itself may be relatively unaffected.

Hyperbilirubinemia

The hazards of hyperbilirubinemia in the newborn are well known. As compared to the healthy full-term infant, the high risk newborn is at greater risk for kernicterus if prematurity, sepsis or acidosis are present. Phototherapy,[4,5] which converts the toxic (indirect-reacting) bilirubin to nontoxic by-products is now generally used in all high risk prematures when the serum level exceeds 5-6 mg%.

Prematurity

The premature infant is at risk for a variety of pathologic problems which are directly related to immaturity. Increased risk for infection and for RDS are examples of pathologic problems which can have a major impact on the potential for survival as well as for quality survival. Intraventricular (intracranial) hemorrhage (IVH) a very frequent autopsy finding in premature infants, is related to immature development in the brain itself. The risk for IVH increases with increasing prematurity and is probably a response to perinatal hypoxia.[6]

In contrast to these pathologic problems, there are other frequent problems in the premature which are "physiologic" rather than pathologic. Although these physiologic problems, such as hypothermia and dehydration, can have a devastating effect on survival and on developmental outcome, they also can be *totally* prevented by appropriate early management.

Hypothermia (cold stress) has already been discussed. Dehydration is a frequent problem because the premature newborn has a decreased ability to excrete a concentrated urine when compared to the full-term newborn or young infant.[7] Because a greater urine output is thus required for any given solute load, the premature infant will continue to excrete large volumes of dilute urine *even in the presence of increasing dehydration.* After the first one-two days of life, therefore, the small premature will ordinarily develop significant dehydration unless supplemental parenteral fluids are provided. As with cold stress, the end result of dehydration is a secondary metabolic acidosis and, ultimately, a further decrease in the potential for survival and/or for quality outcome.

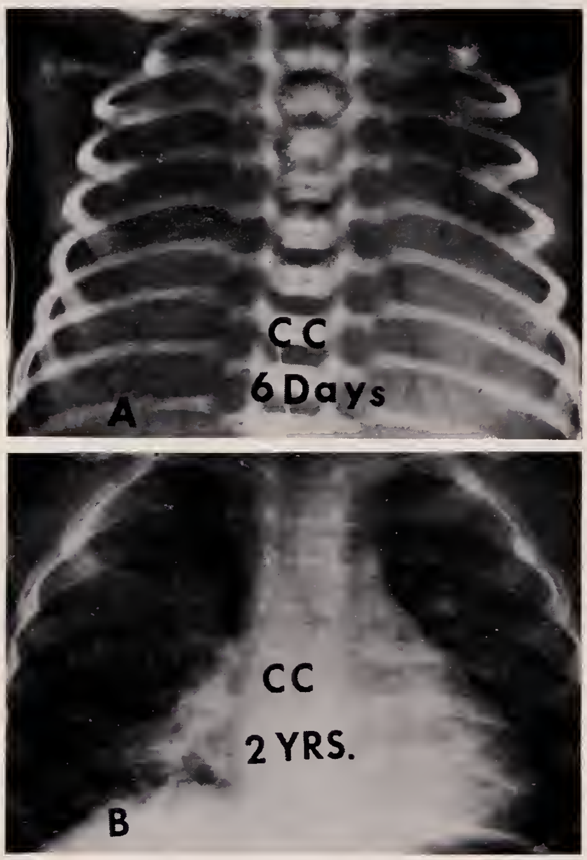
Respiratory Distress Syndrome

Considerable evidence is now available to confirm that assisted ventilation does in fact increase survival from RDS.[8,9] The major change in our approach to assisted ventilation during the past three years has been the introduction of positive end-expiratory pressure, either by: (1) continuous positive airway pressure (CPAP) a system for maintenance of a positive end-expiratory pressure throughout expiration while the patient is breathing spontaneously;[10] or (2) PEEP a system for continuous positive pressure which combines IPPB with positive end-expiratory pressure.[11] By either method, intra-alveolar pressure is maintained above a critical closing level, a greater number of terminal airways remain expanded, and oxygenation can be significantly improved.

The typical patient with severe RDS will have very adequate oxygenation or even hyperoxygenation in the first few hours of age even through critical hypoxia may later occur. Acceptable oxygenation in the first eight to 12 hours of life, therefore, does not preclude the development of critical hypoxia within the next eight-12 hours of life. By intervening with an appropriate level of assisted ventilation *prior* to the occurrence of hypoxia ($PaO_2 < 40$ mm Hg), the morbidity and mortality of severe RDS have been considerably improved.

Opacified or nearly opacified lung fields by thoracic roentgenogram always indicate impending clinical deterioration and, therefore, a need for assisted ventilation. Depending on the degree of prematurity (Table 3), a reasonable potential for survival exists independent of severity of the initial roentgenograms if assisted ventilation is begun as soon as required by the clinical condition.

The patient illustrated in the Figure is representative of our severe RDS group requiring assisted ventilation. Transported to the NICU by fixed wing aircraft at age 24 hours with increasing respiratory distress and nearly opacified lung fields, this 2100 gram premature was begun on assisted ventilation at age 32 hours; 14 days of assisted ventilation and a total of 55 days of 0_2 therapy were required. Although tachypnea and mild retractions were present after hospital discharge, these findings had resolved by one year. At age two years, he is developmentally normal and has no respiratory symptoms. The significance, if any,



Figure—2100 gram premature. Assisted ventilation was begun at age 32 hours and required for 14 days. Total duration of 0_2 therapy was 55 days. The lung fields were nearly opacified within the first 24 hours of life and totally opacified by three days. A. (top) The lung fields are totally opacified so that cardiac and diaphragmatic borders cannot be identified. Extensive air bronchograms are present. B. (bottom) No respiratory symptoms have been present since age one year. Typical long-term roentgenographic changes are present, however, with extensive bilateral interstitial infiltrates and mild generalized hyperexpansion. This patient also has partial right middle lobe atelectasis and significant right upper lobe hyperexpansion.

of long-term roentgenographic changes (interstitial infiltrates and/or hyperexpansion) in 68% of our assisted RDS patients is not known at the present time.[12]

In addition to all the well-known ill effects of hypoxia, critical hypoxia (arterial $PaO_2 < 20$-30 mm Hg) must be avoided in the newborn with RDS for two additional and compelling reasons. First of all, critical hypoxia (with severe acidosis) may impair surfactant production, thereby worsening severity of the RDS and producing further lung damage.[13] Secondly, as indicated earlier, the occurrence of hypoxia in the premature newborn correlates closely with the subsequent development of IVH. Consequent to our improved ability to ventilate the premature newborn with RDS, it is now unusual for these infants to die unless critical hypoxia and subsequent IVH have occurred.

Disseminated Intravascular Coagulation (DIC)

DIC, often in association with severe acidosis, is another major complication of hypoxia. Although classically associated with gram negative sepsis and shock in the older patient, 90% of our DIC cases have been related to severe hypoxia and acidosis. In either case, failure to promptly correct the precipitating problem may lead to a generalized release of thromboplastin, a transient hypercoagulable period and a subsequent depletion of coagulation factors, DIC being the end result. Although DIC can be successfully treated by heparinization alone in the early phase, exchange transfusion with fresh whole blood is necessary when the coagulation factors have been "consumed" and active bleeding is present.[14]

Severity of the precipitating causes of DIC are such that we expect significant developmental abnormalities in the few survivors. From a quality survival point of view, therefore, the only satisfactory approach to DIC is prevention of the cold stress, hypoxia and acidosis, or gram negative sepsis which allows DIC to develop.

Necrotizing Enterocolitis (NEC)

NEC, a relatively recently recognized disease, occurs predominately in prematures and is characterized by an extensive transmural, necrotizing, inflammatory process that may affect both the small and large intestine.[15] The incidence rate for NEC, expressed as a percentage of premature newborn admissions, will vary with severity of the associated medical problems in these high risk newborns. Thus, although our incidence rate was

9% over the past three years, the incidence rate could be 1% or less in a totally unselected group of premature newborns.

The etiology of NEC has not yet been clarified. Although umbilical catheters, exchange transfusions, and sepsis have all been frequently incriminated, they do not provide an adequate explanation. At the present time, the best explanation is that NEC occurs as a secondary response to a period of hypoperfusion of at least a portion of the small and/or large intestine. At least in some of the premature infants, this period of hypoperfusion may well be related to a major perinatal stress, i.e. birth asphyxia, hypothermia or severe hypoxia and acidosis from any cause.

Survival is primarily related to severity of associated medical problems. In those requiring surgical intervention for peritonitis and/or perforation, however, survival may be determined by the length of remaining small intestine after resection of the necrotic segment.

Surgical Conditions

Approximately half of the 88 cardiac deaths occurred in conditions for which palliative and/or corrective surgical procedures are available if early diagnosis and therapeutic intervention can be achieved prior to onset of clinical deterioration.[16] In the two major groups of symptomatic heart disease in the neonate, coarctation of the aorta and complete transposition of the great vessels, survival rates were only 47 and 67%, respectively. Since life-saving surgical procedures are available for both defects, further improvements in survival rates will depend primarily on earlier recognition and therapeutic intervention.

Corrective surgical procedures are available for virtually all of the non-cardiac surgical problems of the neonate. Further improvements in the overall 73% survival rate will also depend on earlier recognition and therapeutic intervention. In almost all such patients, decompression of the gastrointestinal tract by nasogastric suction is an integral part of the early management.

Discussion

Optimal management of the high risk newborn requires an increased level of newborn care. Although an intermediate care (regional) facility may be very appropriate for many high risk newborns, an intensive care facility (defined as having physicians in attendance 24 hours a day) is essential for optimal management of, for example, the small premature or the RDS patient requiring assisted ventilation. When a critically-ill newborn can be anticipated, the optimal approach may often be to electively transport the mother prior to delivery rather than have to later provide emergency transport for the critically-ill newborn.

An essential part of any NICU is a readily available emergency transport system. As is the case for our NICU, such a system should include a nurse and physician trained in emergency neonatal care who travel from the NICU to the primary hospital, by ambulance for distances less than 60-70 miles and fixed wing aircraft for longer distances, and provide all necessary emergency support during transport. Since optimal emergency neonatal transport is best achieved by providing appropriate care during transport rather than by simply providing high speed transport, current efforts are being directed toward equipping our ambulance and planes for complete care enroute, including complete capabilities for assisted ventilation.

Optimal utilization of neonatal centers and the achievement of continuing improvements in neonatal mortality and quality survival rates require ongoing programs in continuing education at the primary hospital level. Under the sponsorship of the Great Plains Organization for Perinatal Health Care, programs at the community hospital and regional center level are becoming more and more available to the nurses and physicians responsible for primary care of the high risk mother and/or newborn and for recognition and early management of all high risk situations.

The considerable financial and health care delivery investment required for neonatal intensive care cannot be justified unless an appropriate increase in quality survival can also be defined. Although currently available developmental outcome results indicate a relatively discouraging potential for quality survival of the high risk newborn, these studies reflect standards of care of 10-15 years ago. In a recent report of developmental outcome in 131 prematures of less than 1500 gram birth weight,[17] for example, although only 30% were completely normal at 10-12 years of age, many principles of neonatal intensive care now considered to be essential to quality survival had not yet been defined and put into practice. Thus, many of these prematures had been exposed to the liberal use of oxygen without adequate monitoring of arterial PO_2, resulting in a 60% incidence of at least some degree of retrolental fibroplasia. Further, although early feeding is now known to be of critical importance in the premature, none of this group received even minimally acceptable caloric intakes in the first weeks of life. Although it is anticipated that early achievement of optimal nutrition in the small premature, including the use of hyperalimentation when necessary, will improve quality survival, these feeding changes are too recent to allow for any long-term developmental follow-up information at this time. Nevertheless, the preliminary developmental outcome data is encouraging.

Evaluations of developmental outcome in survivors admitted to our NICU cannot be considered final until the children are approximately 10 years of age. Preliminary results, however, indicate marked improvements in frequency of normal developmental outcome as compared to the earlier studies. In a recent evaluation of 50 unselected survivors of neonatal intensive care born in 1970, for example, developmental assessment at age two years revealed that 66% were developmentally normal, 25% were "borderline" and 9% were "retarded." Almost identical developmental outcome results have also been obtained at an average of 2.5 years in survivors of severe RDS requiring IPPB.[12]

The evaluation of outcome in survivors of severe RDS must include pulmonary as well as developmental status. Despite the occurrence o radiologic and/or oxygenation abnormalities i about 67% of our survivors, 91% have had n apparent pulmonary symptoms beyond one yea of age.[12] Since survival in RDS patients requirin assisted ventilation is a relatively recent achievement, however, it is not yet possible to relat these asymptomatic radiologic and oxygenatio abnormalities to any potential respiratory difficulties in their adult years.

The potential for normal developmental outcome of the high risk newborn is, obviously, stil significantly less than that of the healthy ter newborn. The improving frequency of normal development does, however, indicate that prematurity and severe RDS are not inherently incompatible with normal development and does justif continued efforts to improve recognition and management of all high risk newborns.

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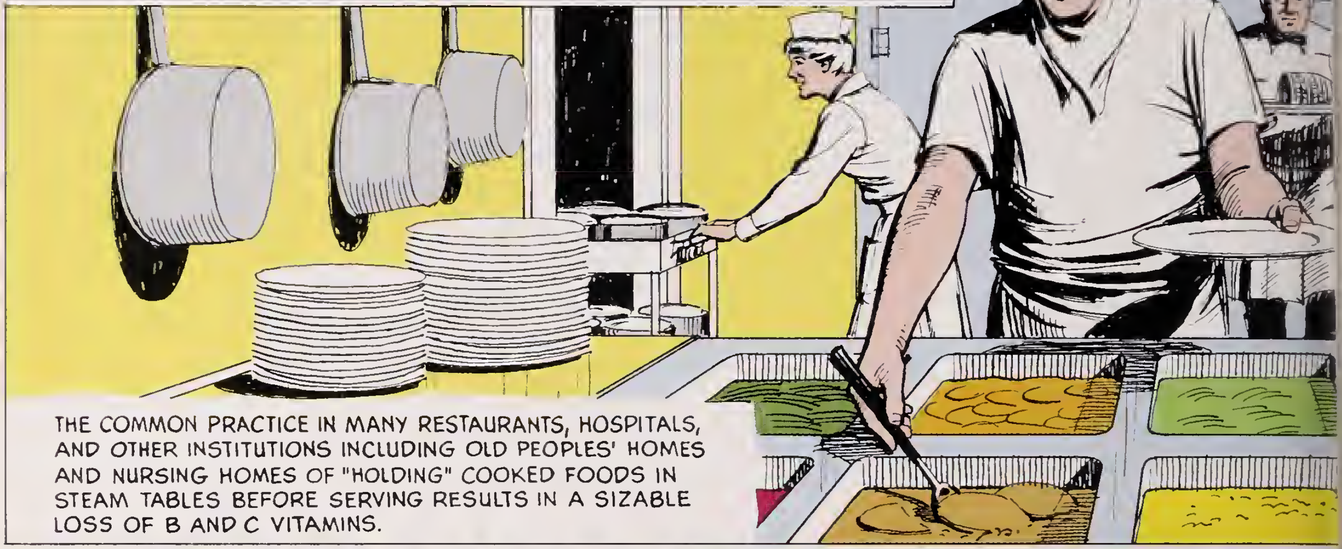

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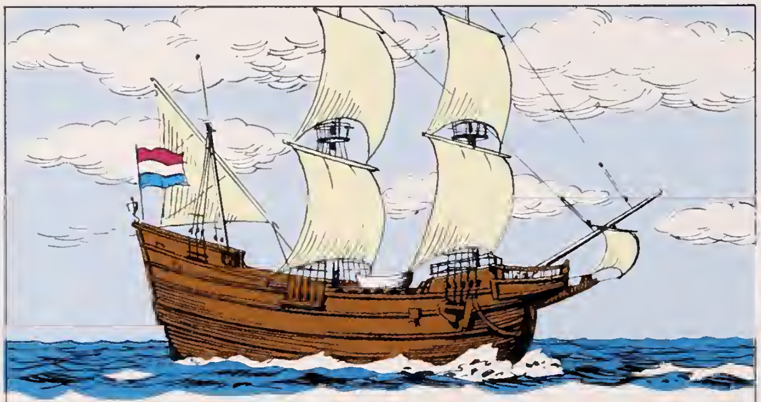

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A Plea for the Routine School Examination of Children for Spinal Deformity

ROBERT B. WINTER, M.D.* AND JOHN H. MOE, M.D.*

A program is proposed wherein school children in the state of Minnesota will ve routine examination of the spine at the ages of 10, 11, 12, and 13. This amination will be performed in the schools by the school nurses and physical ucation teachers. All children with abnormalities detected on this routine examation will be referred to their family physician for further evaluation and Xray. ose individuals having a curve detected to be referred to appropriate physicians medical centers for definitive treatment. With this program we should achieve level of early detection and treatment program which will avoid the need for ajor, expensive, and sometimes dangerous surgery.

HE MILWAUKEE BRACE, developed in 1945,[1] as proven in 1970[5] to be an effective method of n-operative treatment of idiopathic scoliosis. his report by Moe and Kettleson clearly indicated at the treatment results were good only if the rve was detected early, the brace applied omptly, maintained until the completion of owth, and removed gradually.

On the other hand, attempts to treat large and vere curvatures with the Milwaukee brace have oven routinely fruitless, so that surgical correcon and fusion remain the only answer for such rves.[7] Early detection and early non-operative eatment will spare hundreds of children the need r a major operation. When a method of treatent is available which will prevent serious dermity from developing and a major operative ocedure from being necessary, then physicians e morally obligated to detect the cases early nd to apply this form of treatment promptly.

Early Detection

The goal should be the detection of curves hile they are small, for treatment with the Milaukee brace can be effective only if begun before e curves have reached 40 degrees. Results of eatment are better when the treatment begins ith the curves between 20 and 25 degrees. Recgnition of a curve as mild as 25° is difficult on routine standing observation of the back.

These curves appear most commonly at the age of 10-12 when children are shy so, except when swimming in the summer, parents seldom see their children undressed.

Detection of curves of this mild nature is easy with a simple but special examination of the back. The physician should look at the bare back, noticing the level of the shoulders, the level of the hips, and the prominence of one or both shoulder blades.

Most important, he should have the child bend forward toward him as he looks straight down the back. The two sides of the chest should be absolutely symmetrical. If one side is higher a curvature is present, providing the child has bent forward correctly. The child must bend to a right angle at the hips with both arms dropping straight down from the shoulders and the finger tips together, otherwise he may twist his back and give a false impression of a curvature. This is such a reliable technique that curvatures as small as 5-8 degrees can be seen (Figure 2B).

How Can This Be Accomplished?

If all children had this back examination as part of an annual physical examination, the ideal would be accomplished. Unfortunately, a large share of children do not see a physician for routine yearly examination. Even more unfortunately

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*The Scoliosis Service of Gillette Children's Hospital.

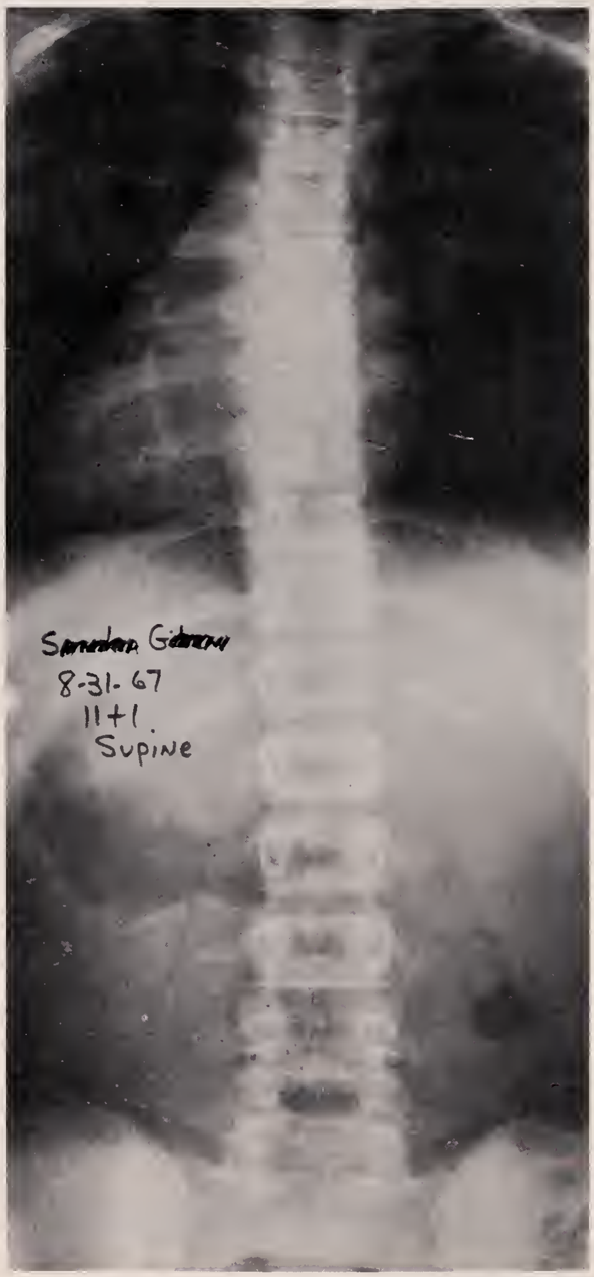
[redacted]
8-31-67
11+1
Supine

Fig. 1-A—An anterior-posterior supine roentgenogram of the spine of an eleven-year-old-girl shows no curve. A slight rib hump had been noted clinically, but unfortunately the Xray was not taken standing. The patient and family were informed "there is nothing to worry about."

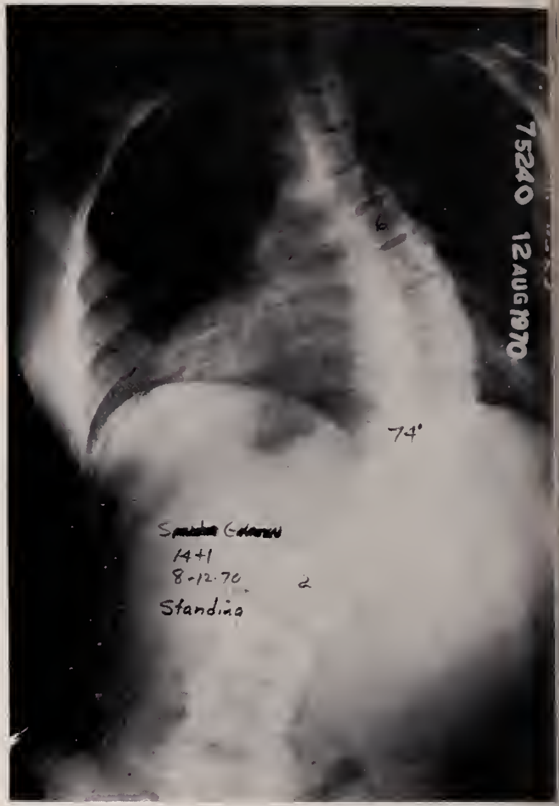
75240 12AUG1970
74°
[redacted]
14+1
8-12-70
2
Standing

Fig. 1-B—The same girl three years later. She n has a severe 74° scoliosis requiring surgical correcti This marked progression could have been prevented proper early treatment.

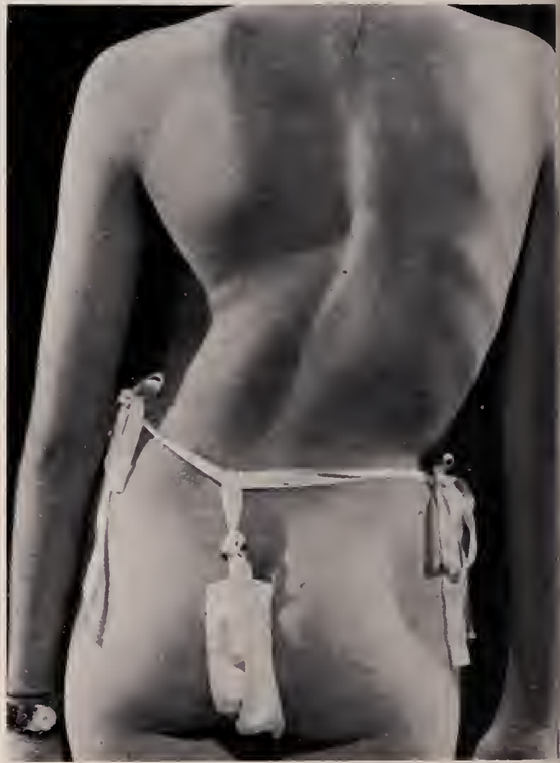

Fig. 1-C—A posterior photograph at age fourte showing the severe deformity.

hen seen for such examination, it is customary examine the eyes, the ears, the lungs, the heart, e stomach, the reflexes, but not the back. herefore, we recommend that back examination, reening program, be done in the school system, r the school is one place where all the children e available for screening on a routine basis. hool examination has proven rewarding in the rly detection of eye and ear problems and their ccess has been sufficiently great that these pro- ams have been continued and are a part of the gular school program.

Approval for such screening has been given by e Minnesota State Medical Association.

School Examination Program

Since the most vunerable age for idiopathic oliosis is the years 10 to 13, we propose that oth boys and girls between these ages be exam- ed on a routine basis. Both may have the con- ition, although the percentage is higher in girls.

Examinations could be done by the school urses in their offices or by the physical education achers in the physical education classes. Screen- g can be performed in a more rapid fashion if rge numbers of children are available in one pace at one time. In a group, the time may be o more than 30 seconds per screening examina- on.

If a possible abnormality is detected, the child ill be given a slip of paper to be taken home and o be given to the parents or guardian. This paper ill recommend that the child be seen by the family physician or pediatrician to evaluate the possible abnormality by an examination that includes a standing Xray for curvature. This will result, of course, in a fairly large number of children coming to the physician for re-examination, and for the anteroposterior standing Xray. If a curvature is present, the physician will probably refer the child to an orthopaedic surgeon, or where orthopaedic consultation is not available, or where financial considerations would require free examination, to the Crippled Children Field Clinics, the University of Minnesota, or the Mayo Clinic.

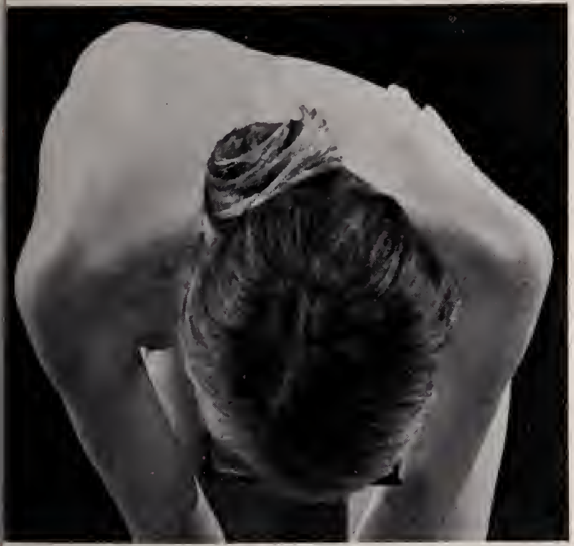

Fig. 1-D—A photograph taken in the foreward bend- ing position. This graphically demonstrates the rotation of the rib cage.

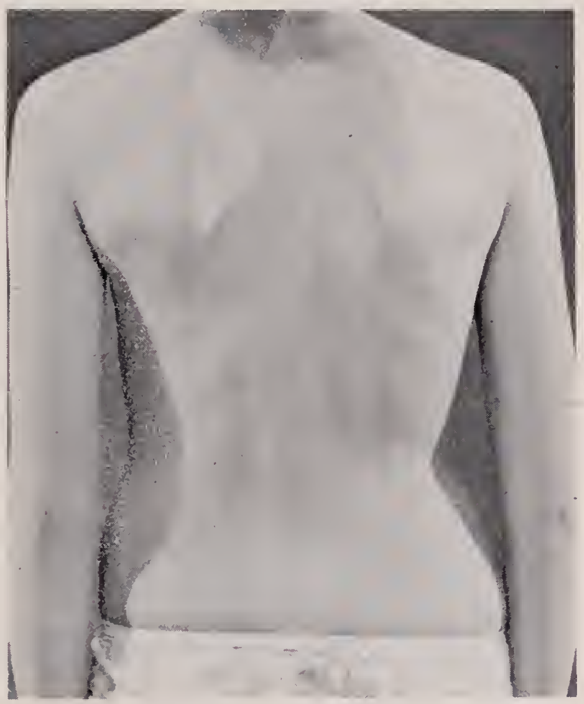

Fig. 2-A—The posterior standing photograph of a twelve-year-old-girl. No deformity can be seen.

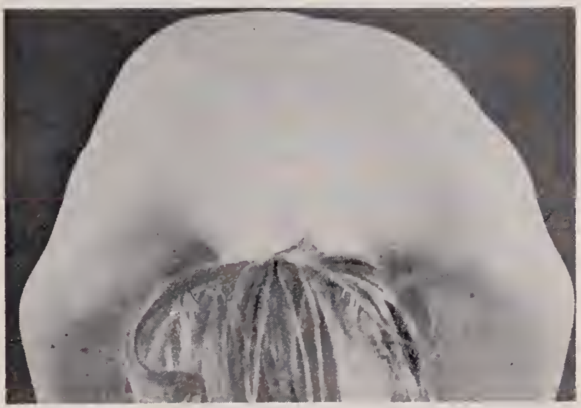

Fig. 2-B—The same girl photographed in the foreward bending position. The right thoracic rib hump can clearly be seen. She has a 10° right thoracic scoliosis. Treatment was not necessary at this time, but should her curve increase, brace treatment will be started.

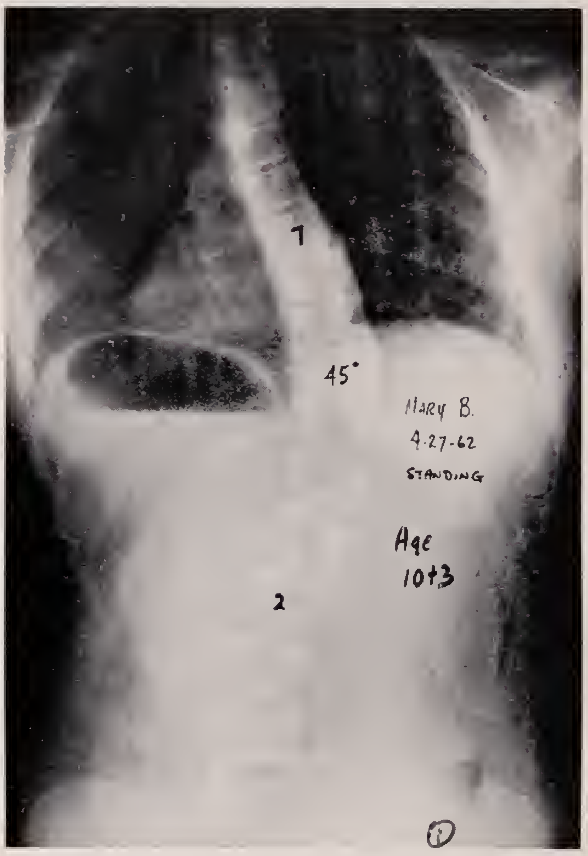
7
45°
Mary B.
4-27-62
STANDING
Age
10+3
2
①

Fig. 3-A—A ten-year-old girl with a 45° idiopathic scoliosis. Milwaukee Brace treatment was started at this time.

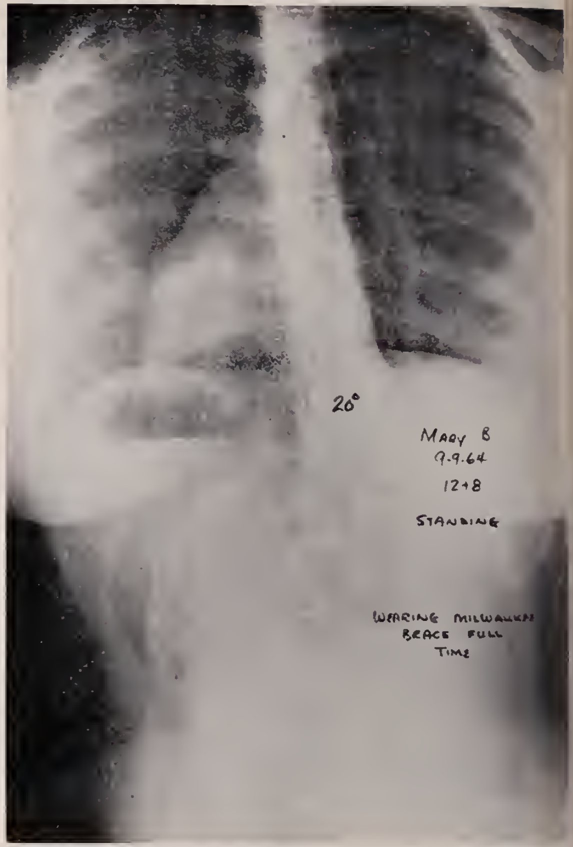
20°
Mary B
9-9-64
12+8
STANDING
WEARING MILWAUKEE BRACE FULL TIME

Fig. 3-B—Two years later, her curve has not onl been kept from progressing, but has been corrected t 20°.

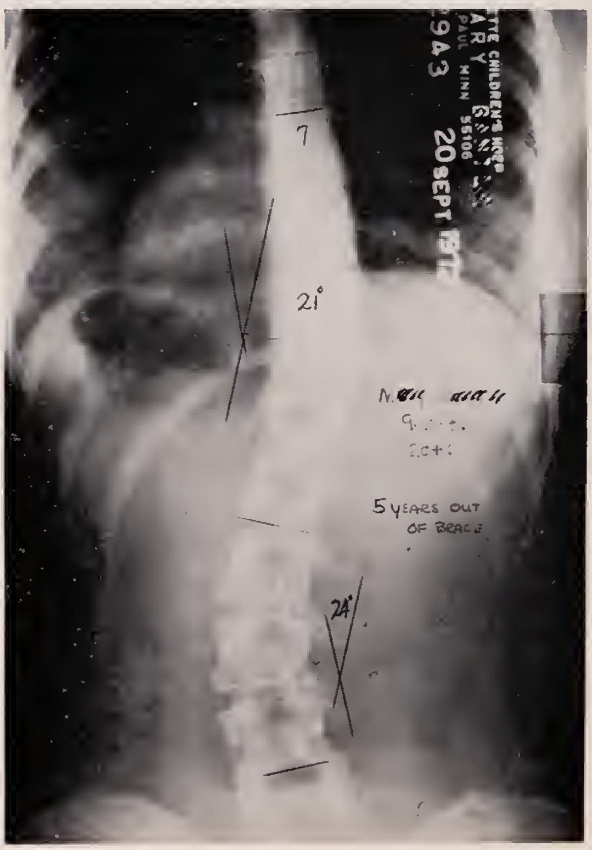
TE CHILDREN'S HOSP
PAUL MINN 55106
943
20 SEPT
7
21°
5 YEARS OUT OF BRACE
24°

Fig. 3-C—At age 20, five years after the brace was removed, her curve is still 21°.

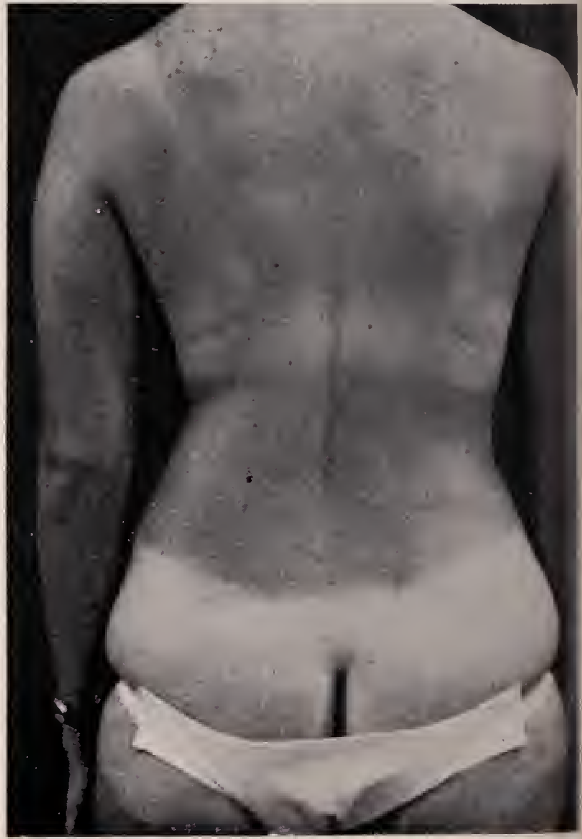

Fig. 3-D—A posterior photograph at age 20.

These curves are progressive during growth and e presence of a small curve at age 11 means at this child will probably develop a large curature by the age of 15 if treatment is not instited. Progressive curvatures must be treated.

X-ray Examination

The obtaining of adequate Xrays is critical in e evaluation of spine deformity. The proper ray *must be taken standing* because early rvatures may disappear when the child is ing down. The Xray should be a single ray which shows the entire spine from the pper thoracic to the lower lumbar area. A 14″ 17″ film should be taken with the top of the lm at the top of the shoulders and the bottom f the film at the upper pelvis. The tube should e centered half way between the top and bottom f the film. The child must be standing with the nees straight and not in a slouched posture.

The normal spine should be absolutely straight. Any amount of lateral curvature is abnormal on he standing Xray in a child. Measurement of the Xrays is left to the orthopaedic consultant since e is familiar with the very particular and precise measurement technique required.

Discussion

Such a program has been proven so successful in Delaware during the past five years, that there are virtually no school children in Delaware that require surgical correction and fusion for idiopathic scoliosis. Almost all curves have been detected early and have responded to appropriate non-operative treatment.

Idiopathic scoliosis is not a rare disease. Surveys of large population masses have found curvatures of 5 degrees or more[2,6] are found in from four to nine percent of the population. A mild curve of this nature becomes progressive, can cause deformity and disability. It is our goal to find and treat these progressive curvatures. Failure to understand the progressive nature of these curvatures has been a major factor contributing to late referral for severe deformity. One of the saddest problems in orthopaedics is to see a child come with a severe curve requiring surgery with Xrays taken many years before showing a mild curve that could have been easily treated with a brace.

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Minnesota State Medical Association
Annual Meeting

Sessions of the House of Delegates

Presentation of credentials by Delegates to the edentials Committee will be held in the Foyer the Radisson Duluth, Wednesday, May 15, 74, noon—1:00 p.m. The first session of the use of Delegates will convene at 1:00 p.m. in e Great Hall of the Radisson Duluth. The sec- d session will convene at 2:00 p.m. in Paulucci all, at the Duluth Arena, Friday, May 17, 1974.

Hearing of the Reference Committees

Hearings of the reference committees will con- ne at 7:30 p.m., Wednesday, May 15, at the adisson Duluth, in the following locations:

1. Medical Practice	Great Hall I
2. Medical Economics	Great Hall II
3. Medical Organization	Poolside
4. Professional Relations	Forest Suite A
5. Officers and Councilors	Forest Suite B

Awards Dinner

The golf and tennis tournaments awards dinners will be combined this year. The Awards Dinner will be held at Northland Country Club 7:00 p.m., Wednesday, May 15, preceded by cocktails at 6:00.

President's Reception and Annual Banquet

The President's Reception which will be held in the Moorish Room of the Hotel Duluth Thursday, May 16, at 6:00 p.m., will include wine and cheese tasting. A variety of wines and complementary cheeses will be available, and cocktails will be served.

The banquet in the Ballroom of the Hotel Duluth, promises to be a gala affair of enjoyment for all. Twenty-two new members of the Fifty Club will be honored, and the Distinguished Service Award and President's Awards will be given to their deserving recipients. The Southern Minnesota Medical Association will award the best scientific exhibit, and the new President of the Minnesota State Medical Association will be welcomed into office.

SCIENTIFIC PROGRAM (Duluth)
Total: 13.5 credit hours
CRISIS MEDICINE/MEDICINE IN CRISIS

Thursday, May 16, 1974

SESSION I: 9:00-10:00 General Session Area, Arena

CORONARY BYPASS—A RESULT ANALYSIS: The management of coronary heart disease has undergone great change in the past decade and much controversy and confusion continues as to both medical and surgical roles in the treatment of this disease, widely recognized as the leading cause of death in this country. The panel will endeavor to cover the high points in regard to such questions as natural history of the disease, diagnosis and medical management of coronary diseases, which patients should be considered for surgery and how they should be evaluated, the basic surgical methods and the results of surgical therapy. The approach will be principally that of discussion among the panel following a brief introductory outline statement by the moderator. The controversial issues will be covered in depth in so far as time permits.

Session Leader: William D. Kelly, M.D.
Thoracic/Cardiovascular Surgeon
Clinical Professor
University of Minnesota Medical School

Participants: 1. Daniel C. Connolly, M.D.
Cardiologist
Mayo Clinic, Rochester

2. Rolf L. Andreassen, M.D.
   Cardiologist
   Northwestern Hospital, Minneapolis
3. Joseph J. Garamella, M.D.
   Cardiologist
   Thoracic-Cardiovascular Surgery P.A.
   Minneapolis
4. James N. Karnegis, M.D.
   Cardiologist
   Charles T. Miller Hospital, St. Paul

BREAK: 10:00-10:30 Exhibits, free refreshments, exhibit area

SESSION II: 10:30-12:00 General Session Area, Arena

CRISES IN EXTRAORDINARY HEALTH CARE: Extraordinary Health Care is occupying more and more physician time and public attention. Included in this category are the most advanced and dramatic treatments which medicine can offer, among them rehabilitation programs for the very elderly, mobile care units for heart disease patients and the most intensive chemotherapy and surgery for advanced malignancy. Many social, scientific, medical and financial considerations enter into these therapeutic programs. The decision of patient eligibility is often as great a problem as the decision when to cease our therapeutic efforts.

This panel will give a frank, direct and realistic discussion of these major issues, views and perspectives in the areas of special knowledge of the panelists. Each major therapy will be approached from the points of view of:

1. Who really should have extraordinary care and who should not.
2. When can such efforts appropriately be stopped.
3. What considerations, if any, should be given to costs and social crises which may result from our medical efforts.

Moderator: Robert L. Carter, M.D.
Dean, School of Medicine
University of Minnesota at Duluth

Panelists:
1. John N. Najarian, M.D.
   Chief Surgeon
   University of Minnesota Hospitals
   Minneapolis (Transplants and Dialysis)
2. John W. Reynolds, M.D.
   Department of Pediatrics
   University of Minnesota Medical School
   Minneapolis (Neonatal Care)
3. Frederic J. Kottke, M.D.
   Professor & Head Dept. of PM, U of M, Minneapolis
   (Physical Medicine)
4. Jesse L. Steinfeld, M.D.
   Chairman, Department of Oncology
   Mayo Clinic
   Rochester (Oncology, Chemo-therapy)
5. Brian C. Campion, M.D.
   Coronary Unit
   St. Paul-Ramsey Hospital
   St. Paul (Coronary Ambulances & Intensive Care Units)

SESSION III: 12:15-1:45 Great Hall, Radisson

COMMUNICATION CRISES IN MEDICAL MARRIAGES

Speaker: Clark Vincent, Ph.D.
Director, Marital Health Clinic
Behavioral Sciences Center
Wake Forest University
Winston-Salem, NC

Communication Crises in marriage are examined as symptomatic of one or more of four basic problems: (1) insufficient self-love, (2) the failure to accept impressions as *real,* (3) insufficient freedom to be different, and (4) childhood legacies concerning male-female learning models. The concepts of "self-love" and "impressions as real" are used to differentiate between "symptoms" and "problems" in marital communication. Case-history excerpts are presented to illustrate social and sexual sources of communication crises, techniques are discussed for resolving these crises.

SESSION IV: 2:00-3:00 Meeting Rooms, Arena

1. CRISES IN OBSTETRICS: Meeting Room 1.

Ten major crises in obstetrics will be presented, backed up by printed material based on the presentation, with space provided for notetaking; to be passed out to those attending the workshop.

These crises are:

1. Severe pre-eclampsia—eclampsia
2. Abruptio placenta
3. Prolapsed cord
4. Primilaparous breech
5. Acute "fetal distress"
6. Placenta previa-accreta
7. Postpartum convulsive seizures
8. Ectopic pregnancy
9. Episiotomy hematoma & breakdown
10. Ruptured Uterus

Participants:

1. Jack E. Wall, M.D.
   Associate Clinical Professor
   University of Minnesota Medical School
   Duluth
2. Bruce F. Williams, M.D.
   Clinical Professor of Obstetrics & Gynecology
   University of Minnesota Medical School
   Duluth

2. LOVE IS TO GROW ON: Meeting Room 4.

"Love is to Grow On" is a 45 minute multimedia presentation utilizing three screens, four projectors, a tape recorder and personal comments. What does a physician advise parents of a newborn baby which is abnormal, e.g. Downs Syndrome? The film compares children in institutions with those raised in their own homes and shows what can be done in a community by proper stimulation and education. The film will be followed by a panel discussing the crisis situations related to parents and physicians and society in the care of retarded and other exceptional children.

Participants:

1. Joseph L. Norquist, M.D.
   Family Physician
   St. Paul
2. Eunice Davis, M.D.
   Pediatrician, Chief, Child Development Section
   St. Paul-Ramsey Hospital
   St. Paul

3. RECTAL AND COLONIC POLYPS—Recent Advances in Diagnosis and Management: Meeting Room 5.

From—Division of Colon-Rectal Surgery
Department of Surgery
University of Minnesota, Minneapolis

Moderator: Carl E. Christensen, M.D.
Proctologist
Medical Fellow in Surgery
U of M School of Medicine, Minneapolis

The first presentation of this two part session will be *Diagnosis and Management of Rectal Polyps.* The pathological spectrum encompassing the term rectal polyp is wide and controversial. The conflicting data surrounding the polyp-cancer sequence and the semantical arguments emanating from the surgical pathology add to the confusion. This discussion will attempt to present a logical and workable diagnostic and therapeutic approach to the problem of rectal polyps and to place into proper perspective the role of the surgeon.

The second part will deal with *Polypectomy Through Fiberoptic Colonscope.* Since the introduction of the fiberoptic colonscope for clinical use several years ago, there has been rapid improvement in the design of the instrument and considerable skill acquired in its handling. Initially used solely as a diagnostic modality, it is now frequently used for the biopsy of colonic lesions and snare-excision of colonic polyps. At the University of Minnesota Hospitals, one hundred and seventy polyps were removed through the fiberoptic colonscope from one hundred and forty patients in an 18 month period of time. There were four post-operative bleeding episodes, one requiring blood transfusion. There was one delayer perforation of the sigmoid colon from fulguration of a small polyp. One patient developed localized pneumatosis coli after the polypectomy. Another patient showed signs of peritoneal irritation but no free perforation. All the procedures were performed in the outpatient clinic except for a four-year-old child from whom a polyp was removed in the operating room. When properly performed the morbidity should be low. Up to the present time, polypectomy through the fiberoptic colonscope should be performed only for clinically benign polyps. When the polyp removed is shown to harbor invasive adenocarcinoma on permament sections, a standard colon resection is indicated.

The two presentations will be followed by a discussion period.

Participants:

1. Graham Fallon, M.D.
   Fellow, Division of Colon and Rectal Surgery
   Department of Surgery, University of Minnesota
   Minneapolis

2. Santhat Nivatvongs, M.D. and Stanley M. Goldberg, M.D.
both of the Division of Colon and Rectal Surgery
Department of Surgery, University of Minnesota
Minneapolis

BREAK: 3:00-3:30 Exhibits, free refreshments, Exhibit Area

SESSION V: 3:30-5:00 General Session Area, Arena

PHYSICIANS' PERSONAL CRISES:

The implications of the four basic problems discussed during the luncheon presentation will be examined in greater depth and with specific reference to the physician's ongoing quest for identity and sanity at a time when he is expected to be all things to all people. These implications include: (1) pressures *on* and *from* his personal marital/sexual life, (2) his use of the medical-practice model when serving as a sexual/marital health consultant for patients, (3) the importance of authoritativeness, (4) an understanding of his own sources of self-love, and of his particular style or pattern of defenses and coping behavior.

A general session featuring one main speaker.

Speaker: Clark Vincent, Ph.D.
Wake Forest University

Friday, May 17, 1974

SESSION VI: 8:30-10:45 General Session Area, Arena

SYPOSIUM ON TRAUMA: Presented by the Minnesota Chapter of the American College of Surgeons

Session Leader: Martin A. Adson, M.D.
Consultant in Surgery, Professor of Surgery
Mayo Medical School
Rochester

8:30 Evaluation of Thoracic Trauma:
James V. Maloney, Jr., M.D.
Professor of Surgery
UCLA Medical Center
Los Angeles

8:45 Fluid and Electrolyte Balance in the Traumatized Patient:
James R. Pluth, M.D.
Consultant in Surgery, Assistant Professor of Surgery
Mayo Medical School
Rochester

9:00 The Shock Lung:
Edward W. Humphrey, Jr., M.D.
V.A. Hospital
Minneapolis

9:15 Assessment and Treatment of Central Nervous System Trauma:
Burton M. Onofrio, M.D.
Consultant in Neurologic Surgery
Assistant Professor of Surgery
Mayo Medical School, Rochester

9:30 Evaluation of Blunt Abdominal Trauma:
John F. Perry, Jr., M.D.
Thoracic Surgeon, Professor and Director
St. Paul Ramsey Hospital, St. Paul

9:45 Panel Discussion

BREAK: 10:15-10:45 Exhibits, free refreshments, exhibit area

SESSION VII: 10:45-noon

SYMPOSIUM ON EMERGENCY SERVICES: Presented by the Minnesota Chapter of the American College of Surgeons

Session Leader: Martin A. Adson, M.D.
Consultant in Surgery, Professor of Surgery
Mayo Medical School, Rochester

Regionalization of Trauma Care—The Illinois Experience:
David R. Boyd, M.D.C.M.
Chief, Bureau of Emergency Medical Services and Highway Safety
Illinois Department of Public Health

Progress in Minnesota:
William C. Woyda, M.D.
Chairman, Committee on Emergency Medical Service
Minnesota State Health Department

SESSION VIII: 12:15-1:45 Great Hall, Radisson

"DOCTOR, WILL THAT RADIATION HURT ME?":

This increasingly common question is asked of many doctors in a modern world where patients get x-rayed, children watch T.V. and people live near nuclear power plants. Twice since World War II, the use of radiation in medicine has been questioned by the scientific community and has been the focus of public anxiety. The first time was in the early fifties during the fallout controversy. Presently, it is occurring in the nuclear power controversy. In answering the question, "Doctor, will that radiation hurt me?" the physician has one of four choices. He can (1) dismiss it quickly by saying, "No, don't worry about it," (2) authoritatively state that the benefit of radiation outweighs the risk, (3) give the patient a short course in radiobiology, or (4) numerically estimate the risks and compare them to other risks.

In this paper, Dr. Linnemann will discuss basic information the physician should know about radiation dose-effect relationships. He will compare the exposures from various sources of radiation. Special emphasis will be placed on the problem of radiation exposure in pregnancy. In short, he will attempt to place in perspective an answer to the question, "Doctor, will that radiation hurt me?"

Speaker: Roger E. Linnemann, M.D.
President, Radiation Management Corporation
University City Science Center
Philadelphia, PA

SESSION IX: 2:00-3:30 Meeting Rooms, Arena

Workshops (to run concurrently)

1. BENEFIT VERSUS RISK IN THE USES OF IONIZING RADIATIONS: Meeting Room 1.
   Moderator: Merle K. Loken, M.D., Ph.D.
   Professor of Radiology
   Director, Division of Nuclear Medicine
   University of Minnesota
   Minneapolis

Participants:
Roger E. Linnemann, M.D.
Philadelphia, PA

Warren Lawson, M.D.
Executive Director
State Board of Health

Eugene Gedgaudas, M.D.
Professor and Chairman
Department of Radiology
University of Minnesota, Minneapolis

Donn G. Mosser, M.D.
Radiation Therapist
Northwestern Hospital, Minneapolis

The various uses of radiation in the practice of medicine as well as in power production will be discussed. The panel will attempt to provide a perspective of benefit derived versus the risks involved from radiation exposure. Each of the participants will be given five minutes to summarize his involvement in radiation utilization. Following will be a perspective presented on present maximum permissible radiation doses for our population and how this relates to the amount of radiation received from environmental sources as well as from the practice of medicine. Consideration will be given to methods of reduction of radiation exposure and possible alternatives to the use of radiation sources in medicine and for power production.

2. THE ACUTE PAINFUL JOINT: Meeting Room 2.
Chairman: Paul Bilka, M.D.
Panelists: Thomas W. Bunch, M.D.
Mayo Clinic, Rochester

Roger S. Colton, M.D.
St. Paul

Gerald T. Mullin, Jr., M.D.
Minneapolis

Krishna Saxena, M.D.
St. Paul

The panelists will discuss the clinical characteristics, diagnosis, and treatment of the acute painful joint. Each panelist will discuss one of the frequently occurring conditions presented as an acute inflammatory synovitis including gout, pseudogout, septic arthritis, especially tuberculous and gonococcal, episodic rheumatoid arthritis, the acute painful shoulder, rheumatic fever. The panelists will discuss their experience in the management of these problems followed by an open discussion with the members of the audience.

Gout—Pseudogout—Thomas W. Bunch, M.D.
Septic Arthritis (especially TB and GC)—Roger S. Colton, M.D.
Painful Shoulder—P. Bilka, M.D.
Nonseptic Inflammatory Arthritis—RA—episodic—and variants—Gerald T. Mullin, M.D.
Rheumatic Fever—K. Saxena, M.D.

3. CRISES INVOLVING CHEMICAL USE, ABUSE OR DEPENDENCY: Meeting Room 3.

This workshop, the responsibility of the Subcommittee on alcoholism and Other Chemical Dependency and of the Health Professionals Drug Abuse Education Project, will deal with drug-related crises for which the physician's help may be sought. But it cannot deal in depth with all such crises. Which, then, should be considered? Which not? Since those crises involving respiratory depression and cardiovascular collapse are of obvious importance, we shall provide for each physician some appropriate information for study and future reference. But it is just these crises which have attracted the attention of planners of other meetings and programs, so we shall emphasize other things.

One kind of drug-related crisis may be entirely overlooked by the physician and has been little considered in educational programs: the family crisis following, for example, upon parental discovery that a child is using some kind of drug. This sort of thing may be a very real crisis for the physician, and one for which he may be largely unprepared. Another, and sometimes related, crisis involves drug use and the law. We shall spend some time with each of these and with considerations of agencies and programs which may be available to assist the physician in dealing with them in his practice.

Abuse problems often involve licit drugs, sometimes prescription drugs. Ill-advised use of prescription drugs may be traceable to the physician, whose ongoing drug education is usually fragmented by its dependence on pharmaceutical detail men. Adverse drug interactions may be problems; ill-appreciated drug side-effects may become problems by causing clinical conditions unrecognized as drug-related. Those whole problem areas will be considered, with special reference to the emerging role of the Clinical Pharmacist.

Involved are: David Auran, M.D., Chairman,
MSMA Subcommittee on Alcoholism and Other
Chemical Dependency

Robert G. B. Bjornson, M.D.
Co-Director, Health Professionals Drug
Abuse Education Project (NIMH)
Member, MSMA Subcommittee on Alcoholism
and Other Chemical Dependency

Joel Egertson, Executive Director
Minnesota State Alcohol & Drug Authority

Martin Jinks, Pharm.D.
Assistant Professor, Clinical Pharmacy
University of Minnesota & S.. Paul Ramsey Hospital

Marc Kurzman, J.D., R.Ph.
Associate Director
Drug Information & Education Program
University of Minnesota

Robert Reif, M.D.
Director of Medical Education
St. John's Hospital, St. Paul

Member, MSMA Subcommittee on Alcoholism
and Other Chemical Dependency
Member, Advisory Committee, Health
Professionals Drug Abuse Education Project

James Rothenberger
Assistant Director
Health Professional Drug Abuse Education Program
Board of Directors
DEFY (Drug Education for Youth).

Lawrence Weaver, Ph.D.
Professor and Dean
College of Pharmacy
University of Minnesota

Darwin Zaske, Pharm. D.
Clinical Pharmacist
St. Paul Ramsey Hospital
St. Paul, Minnesota
Instructor, Clinical Pharmacy
University of Minnesota

James Anthony
Instructor, Clinical Pharmacy
University of Minnesota, Minneapolis
Faculty Director, Drug Information—
Community Drug Information Program
University of Minnesota, Minneapolis
College of Pharmacy

BREAK: 3:30-4:00 Exhibits, free refreshments, exhibit area

SESSION X: 4:00-5:00 General Session Area, Arena

HUMAN SEXUALITY

Sexual ignorance, fears and guilts are a major diversion of human energy, a cause of human energy disease, and a significant contributor to the intimacy gap between couples. Statistics show that 50-75% of married couples are sexually dysfunctional, while most health professionals rarely question their patients about their sexual health. The significance of these observations is expressed in terms of the emotional, as well as the inherent limitations to the development of human potential that occur when sex is less than a natural function.

The emphasis of this presentation will be upon informational and attitudinal education to help health professionals encourage sexual health—defined as the integration of the individual's intellectual, physical and emotional sexual natures, to the furtherance of communication and love.

Presented by: Richard A. Chilgren, M.D.
Department of Human Sexuality
University of Minnesota
Minneapolis

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Streptococcal Infections Workshop

"The Outlook for Community Control of Streptococcal Infections and Their Sequelae—1974" workshop sponsored by the American Heart Association, the Great Plains Regional Heart Committee of the American Heart Association, and the Minnesota Heart Association will be held in Minneapolis on May 31-June 1, 1974. Sessions will include talks by a nationally recognized faculty as well as two one-half days of workshops. Topics will include newer concepts of the epidemiology and pathogenesis of streptococcal infections of the upper respiratory tract and the skin and their sequelae, rheumatic fever and acute nephritis, school streptococcal control programs, newer concepts in the laboratory diagnosis of streptococcal infections, as well as discussion of streptococcal control in urban and rural populations. This course has been approved for 10 elective hours by the AAFP.

For further information and registration contact: Minnesota Heart Association Office, 4701 W. 77th St., Minneapolis, Minnesota 55435.

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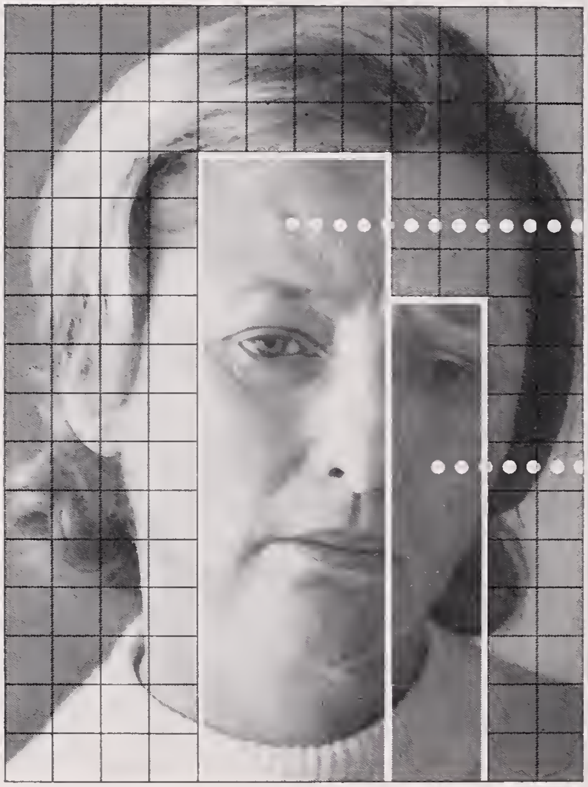
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For further information on this subject, the following references are provided:

1. Henry BW, *et al: Dis Nerv Syst 30*:675-679, Oct 1969.
2. Hollister LE, *et al: Arch Gen Psychiatry 24*:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics 11*:438-441, Sept-Oct 1970.

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References: 1. Reuter, S. H., and Montgomery, W. W.: Arch. Otolaryng. *80*:214-217 (Aug.) 1964. **2.** Osol, A., et al., ed.: The United States Dispensatory and Physicians' Pharmacology, ed. 26, Philadelphia, J. B. Lippincott Co., 1967, p. 171. **3.** Schwartz, A. D., and Pearson, H. A.: J. Pediat. 78:558-560 (March) 1971.

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President's Letter

Peer Challenge—Peer Review

PEER CHALLENGE is my problem. Each of us can recall the severe demands imposed by *challenge* from our peers in medical school, in the armed services, in the first year of practice, and in the increasingly complex present. Our careers in medicine can be viewed as series of *challenges* presented by our peers.

As President of the Minnesota State Medical Association, I am confronted by another *challenge* from my peers. You, the members of the association have honored me and *challenged* me to act as the spokesman for you and your policies during the coming year. It is an honor for which I feel unworthy, but it is a *challenge* which I am anxious to meet.

To help me in this *challenge* I have the fine example and accomplishments of Dr. John Regan. He has served with distinction and dignity during the past year. He listened quietly, but added his considered opinions in the course of the discussions. I personally shall miss his monthly vignette printed on this page. Congratulations, John, for a job well done.

The help of each member of the State Association will be necessary if we are to successfully meet the *challenges* which surround us. I expect you to provide me with a continuing review of my performance. I can speak for you to the public, press and the politicians only if we first communicate.

Peer review is our responsibility: one that must be met in the years to come whether it be by our own initiative or in response to public pressure. Even though Professional Standards Review Organization (PSRO) legislation may be repealed, these pressures can not be ignored.

Peer review is a *challenge* we must face. Have we in the past failed to adequately respond to problems within the profession? Others feel we have; they feel we have waited too long to act, have been too protective and unconcerned.

Concern for and protection of our patients must always be our goal, and only in that way can we guarantee the survival of superior medical care. The mechanism by which others will review our performance already exists. We can not abdicate this responsibility. Let us through our societies and committees make the decision to meet this *challenge*.

Bernard Hall M.D.

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Prediction of the Respiratory Distress Syndrome

By Analysis of Cord Protein and Alpha-1 Antitrypsin

RICHARD D. REHM, M.D.;* JOHN FANGMAN, M.D., PH.D.;† JACK STROBEL, M.D.;†
AND SEYMOUR HANDLER, M.D.#

Cord serum protein determinations were performed on 543 consecutive infants. ord alpha-1 antitrypsin levels were determined on 30 of these infants whose cord erum total protein was below 4.6 gm/dl and on 18 randomly selected control ıfants with normal proteins. It was found that 75% of infants with cord serum ıtal proteins of 4.2 gm/dl or less developed IRDS. Fifteen of eighteen infants with RDS had cord serum total proteins of 4.2 gm/dl or less (83%). In infants with ord blood alpha-l antitrypsin concentrations below 1.65 mg/ml, only 30% deeloped IRDS. While infants with IRDS tended to have low alpha-1 antitrypsin vels (7 of 10), a large number of non-IRDS infants also had low alpha-1 antiypsin levels, limiting the predictive value of this parameter.

THE PRESENT STUDY was undertaken to comare the value of cord blood total serum protein nd alpha-l antitrypsin levels in predicting idioathic respiratory distress syndrome (IRDS). land[2] has demonstrated that the serum total proein in cord blood can be used with a significant egree of accuracy in predicting the development f IRDS. Alpha-1 antitrypsin levels have also been emonstrated to be decreased in infants with RDS. Kotas and his associates[3] demonstrated dereased serum trypsin inhibitory capacity in infants ith IRDS and found this useful in predicting not nly the development, but also the severity of the RDS. While the usefulness of the lecithin-sphingomyelin ratio has been demonstrated,[1] the predictive value of the procedure is limited to cases in which amniocentesis can be performed and the time of delivery can be controlled by the attending physician.

Materials and Methods

Umbilical cord blood serum total protein determinations were carried out on 543 consecutive live births between October 1, 1972, and January 13, 1973. Alpha-1 antitrypsin levels were carried out on 30 infants whose cord serum total protein was 4.6 gm/dl or less, and on 18 infants whose cord serum protein was greater than 4.6 gm/dl.

The study group of 543 infants included 100 infants with gestational ages of 37 weeks or less. The birth weights of the population ranged from 666 grams to 4,550 grams. Eighteen of these in-

TABLE
Distribution of Infants in Study by Gestational Age with Average Proteins of Grouped Ages. Proteins Increase with Gestational Age.

	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39-40+
Number of infants	1	0	1	0	2	2	2	1	1	4	4	10	19	53	443
average protein			3.93					4.46			4.90		5.20	5.16	5.89

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fants (3%) had a clinical diagnosis of IRDS. The diagnosis of IRDS was based on the clinical picture of respiratory tachypnea, retractions, grunting respirations, and cyanosis in room air. In nearly all cases of IRDS, chest x-ray findings were consistent with the clinical diagnosis and arterial blood gases demonstrating decreased PO_2 and increased PCO_2 were available. In the two infants with IRDS who expired, the clinical diagnosis was confirmed by postmortem examination. Neither the cord serum protein values or the alpha-1 antitrypsin levels were known by the investigators who made the diagnosis of IRDS. The mean gestational age of the infants developing IRDS w
34.3 weeks and their mean birth weight was 2,18
grams.

Total protein determinations were made on a
infants using the TS meter* with the techniqu
similar to that employed by Bland.[2] All dete
minations were made within two hours of deliver
of the infant. The serum for alpha-1 antitrypsi
determinations was frozen immediately.

Serum trypsin inhibitor activity was measure
according to Lieberman.[4] Trypsin used in thes
studies was a two times crystallized, ethanol pr
cipitated, salt free preparation obtained fro
Sigma Chemical Company in St. Louis, Missour

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*TS Meter, American Optical Corporation, Buffalo, N.Y.

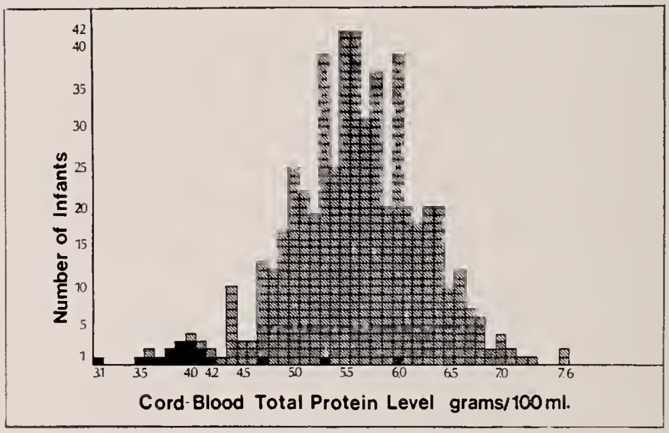

Fig. 1—The above figure shows the number of infants at each cord serum total protein level. Each square represents one infant. Blackened in squares represent infants with IRDS.

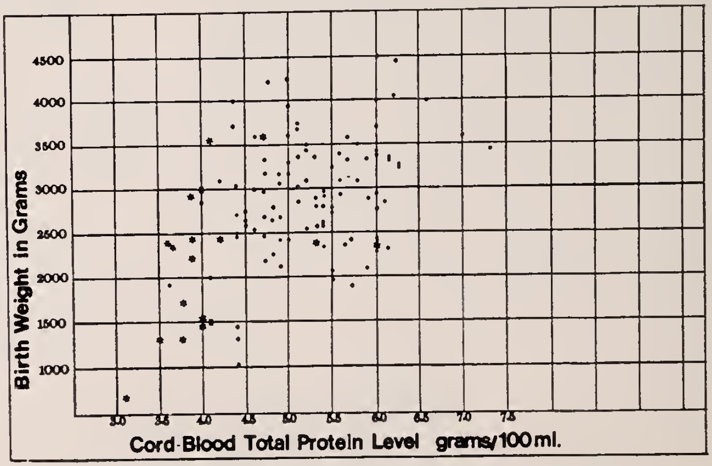

Fig. 2—Increasing cord blood protein values with increasing birth weight. Stars represent infants with IRDS. The 107 infants plotted on this graph, as well as on Figure #3, represent those infants in the study at greater risk of IRDS on the basis of abnormal pregnancy or delivery factors.

ypsin inhibitory activity is expressed as the mg trypsin inhibited per ml of serum.

Results

The range of cord blood serum total protein ncentrations of the 543 infants varied from 3.1 /dl to 7.6 gm/dl with a mean of 5.6 gm/dl. ure 1 shows the distribution of cord serum pro- n values irrespective of gestational age or weight. e Table shows that the mean protein level for ants increased with gestational age.[5] Figure 2 ws the relationship between cord serum total tein and birth weight. Figure 3 shows the ationship between cord serum total protein and gestational age. Low serum protein values occurred in both term and pre-term infants.

The mean level of cord serum total protein in the 18 IRDS infants was 4.1 gm/dl. The mean value of cord serum total protein in the non-IRDS infants was 5.4 gm/dl. This difference is significant at the .05 level.* Of the eighteen infants who developed IRDS, fifteen had a cord serum total protein of 4.2 gm/dl or less. Of the nineteen infants who had a cord serum total protein of 4.2 gm/dl or less, fifteen developed IRDS, an incidence of 79%. One of the three blood specimens from the three infants with IRDS and a cord protein above 4.2 gm/dl was hemolyzed, a

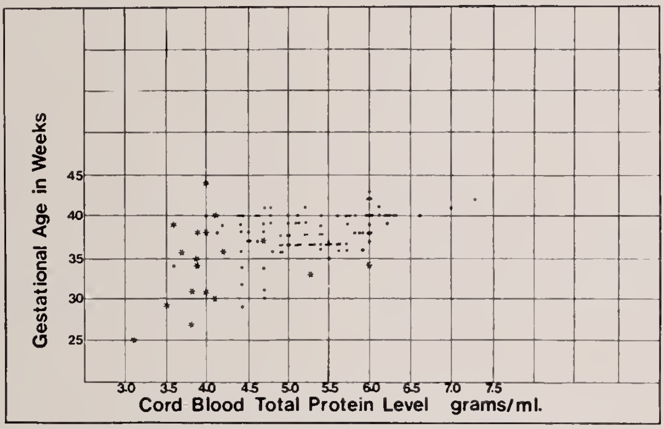

Fig. 3—Increasing cord blood proteins with increasing gestational age. Stars represent infants with IRDS.

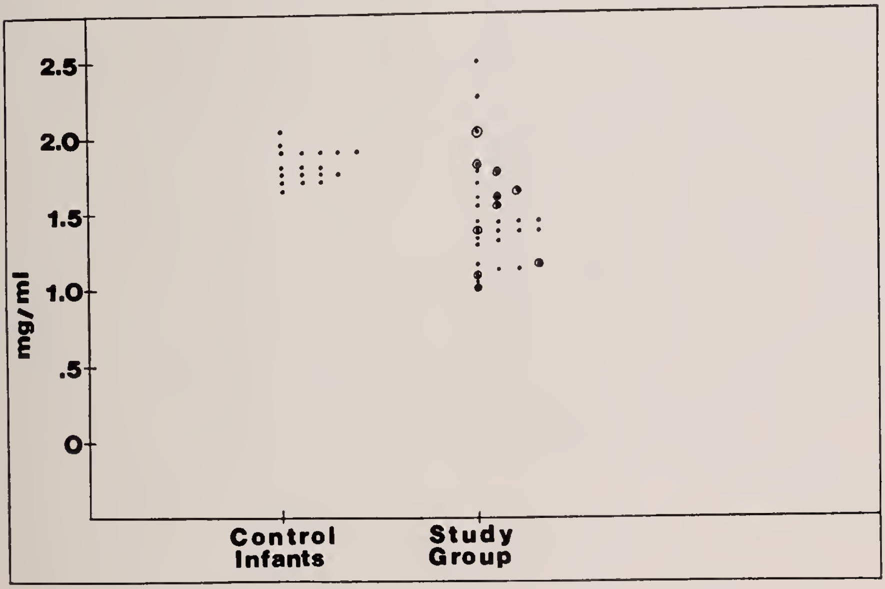

Fig. 4—Alpha-1 antitrypsin levels in mg/ml of the 18 control normal protein level infants and 30 low protein level infants. Circled dots represent infants with IRDS.

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*ne tail T test.

condition which elevates the serum protein as determined by the TS meter. No hemolysis was noted in the other two samples.

Alpha-l antitrypsin levels were determined on 30 of the cord specimens with cord serum total proteins less than 4.6 gm/dl and on 18 randomly chosen infants with cord serum protein concentrations above 4.6 gm/dl (Figure 4). The mean proteins for the two groups were 4.14 gm/dl and 5.70 gm/dl respectively. Alpha-1 antitrypsin levels were determined on 10 infants who developed IRDS,* all of whom had cord serum total proteins of 4.2 gm/dl or less. The mean level of alpha-1 antitrypsin in the infants with a total protein of 4.6 gm/dl or less was 1.50 mg/ml with a range of 1.00 to 2.50. The mean alpha-1 antitrypsin concentration in infants with a protein level below 4.6 gm/dl who developed IRDS was 1.49 mg/ml with a range of 1.00 to 2.03. The mean in infants with a protein level below 4.6 gm/dl who did not develop IRDS was 1.51 mg/ml with a range of 1.02 to 2.50. This difference is not statistically significant. A total of 21 of the 30 infants in the low protein study group had alpha-1 antitrypsin levels below the lowest level found in the control group (1.65 mg/ml). Seven of these twenty-one developed IRDS, or 33%. There were three IRDS infants among the 27 infants above this level for an incidence of 11%.

Discussion

Cord blood serum total protein levels and cord blood alpha-1 antitrypsin levels have previously been shown to be predictive parameters for the development of IRDS.[2,5] In this study, designed to evaluate these two parameters in the same group of infants, cord blood serum total protein levels were found to increase with both gestational age and birth weight. Irrespective of gestational age or birth weight, infants who developed IRDS had significantly lower cord proteins than infants of comparable gestational age and birth weight who did not develop IRDS. In this study, an infant with a cord serum total protein of 4.2 gm/dl or less had approximately an 80% risk of developing IRDS, irrespective of gestational age or birth weight.

Alpha-1 antitrypsin levels of cord blood were not found to correlate with either gestational or birth weight. Although there was a tende for infants with IRDS to have lower alpha-l a trypsin levels than comparable non-IRDS infa the difference was not statistically signific Seven of the ten infants who developed IRDS alpha-1 antitrypsin levels lower than the low control infant (1.65 mg/ml). However, sixt of the twenty non-IRDS infants in the study gr had alpha-1 antitrypsins below this level a Thus, the predictive value of a low cord alph antitrypsin is limited, with only seven infants veloping IRDS out of twenty-three with l alpha-1 antitrypsin concentrations.

Mathis et al.[6] demonstrated a significant re tionship between alpha-1 antitrypsin levels a the severity of the IRDS. Although they stud 34 infants with IRDS, in only seven of th infants was a cord blood alpha-1 antitrypsin le determined. The remaining 27 determinati were made on blood samples obtained during first 48 hours of life. These investigators a demonstrated a fall in alpha-1 antitrypsin w the worsening symptoms of IRDS in babies w had sequential determinations made. Control fants did not show a similar fall in serum alph antitrypsin levels. Their study also demonstra by immunofluorescent techniques the depositi of the alpha-1 antitrypsin in the hyaline me branes. Thus, cord blood alpha-1 antitrypsin c relates most directly with a low total protein a cannot be used in and of itself to predict infant at high risk of developing IRDS.

Kotas et al.[3] suggested using the trypsin inhi tory capacity (TIC) of cord serum to predict fa IRDS. Using a TIC of below 0.65 mg/ml, th found an incidence of IRDS of 87%. A subst tial number of their infants with TIC levels ab 0.65 mg/ml also developed IRDS (i.e. 16 of 4 If the cut-off point (0.65 mg/ml) had been e ployed to predict incidence of IRDS, and th institute either intensive care procedures transfer of such infants to a neonatal intensive c unit, only 56% (20 of 36) of the IRDS infa would have been selected for such care.

While cord alpha-1 antitrypsin levels and c serum total proteins are reported to be useful predicting IRDS in the newborn, no previous stu has compared these two parameters in the sa cord samples. The present study strongly sugge that cord serum total proteins are of greater p dictive value than alpha-1 antitrypsin levels rd blood. Using a cord serum total protein lue of 4.2 gm/dl or less as a cut-off point, % of the infants developed IRDS. Employing cut-off point for alpha-1 antitrypsin of 1.65 g/ml, only 30% of the infants below the level veloped IRDS. While 70% of the IRDS in- its studied did have a low alpha-1 antitrypsin el, many non-IRDS infants also had compar- le low levels.

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*The frozen sera of 8 of the IRDS infants was inadvertently used by lab personnel for other lab tests prior to the alpha-1 antitrypsin determinations.

Technical feasibility of the two tests is another tor in evaluating widespread clinical usage. e TS meter was chosen as the method of deter- nation of cord protein levels because of its e of use, rapidity of determination, reliability, d nearly universal availability. General lab- itory personnel are adequate for use of the TS meter and the cost of the test is small. On the other hand, by present methods, alpha-1 antitrypsin level determination is complex, requiring a sophisticated laboratory. The greater expense of alpha-1 antitrypsin determination must also be considered when using the test as a screening aid.

This preliminary study, demonstrating the usefulness of cord blood serum total proteins in the prediction of IRDS, indicates a need for a larger prospective study to determine general application of the test.

Acknowledgment

Alpha-1 Antitrypsin determinations were performed by Robert C. Wong, Ph.D., Clinical Chemistry Department, North Memorial Medical Center.

Special assistance provided by Miss Wendy Bogeskov, RRA, data collection; and Mrs. Kristi Youngdahl, illustrations.

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Cupid laid by his brand, and fell asleep:
A maid of Dian's this advantage found,
And his love-kindling fire did quickly steep
In a cold valley-fountain of that ground;
Which borrowed from this holy fire of Love
A dateless lively heat, still to endure,
And grew a seething bath, which yet men prove
Against strange maladies a sovereign cure.
But at my mistress' eye Love's brand new-fired
The boy for trial needs would touch my breast;
I, sick withal, the help of bath desired,
And thither hied, a sad distemper'd guest,
    But found no cure: the bath for my help lies
    Where Cupid got new fires—my mistress' eyes*

Shakespeare, "Sonnets," CLIII.

Persistent Truncus Arteriosus

Associated with Tricuspid Atresia

RAJENDRA TANDON, M.D.*; JAMES H. MOLLER, M.D.* AND
JESSE E. EDWARDS, M.D.

Clinical and necropsy findings of a patient with persistent truncus arteriosus coexisting with tricuspid atresia are described. The combination of tricuspid atresia and persistent truncus arteriosus has not been reported previously.

THE ASSOCIATION OF PERSISTENT truncus arteriosus with significant malformations of the atrioventricular valves is uncommon. In asplenia persistent truncus may be associated with an atrioventricular valve characteristic of persistent common atrioventricular canal. The presence in the same patient of persistent truncus arteriosus and tricuspid atresia has not previously been reported. Observation of such a rare occurrence prompts us to record this case.

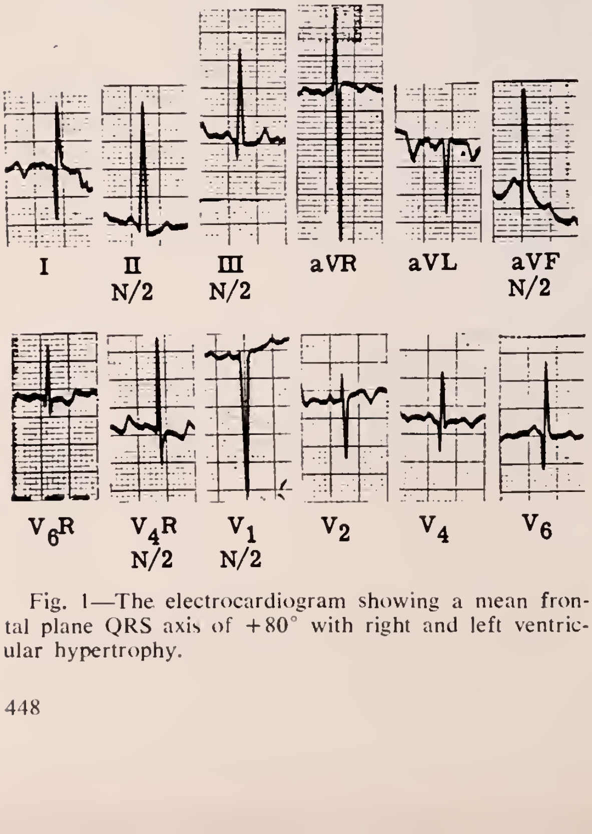

Fig. 1—The electrocardiogram showing a mean frontal plane QRS axis of +80° with right and left ventricular hypertrophy.

Case Report

Clinical Features

At age two months, a male infant with an unrema able family, prenatal, and natal history, was refer to the University of Minnesota Hospitals. A heart m mur was discovered at the age of three days. Subsequen the symptoms were diaphoresis and episodic difficulty breathing associated with intense cyanosis.

Physical examination showed a small, irritable, cryi and dyspneic child. The blood pressure obtained by fl method was 70 mm. in an arm and 100 mm. Hg in leg. The skin was mottled and slightly cyanotic. grade III/VI systolic murmur, heard throughout t precordium, was loudest along the right sternal bord The liver was palpable two fingerbreadths below t right costal margin.

Electrocardiographically, in the frontal plane t mean QRS axis was +80° and the "T" axis +105°. T

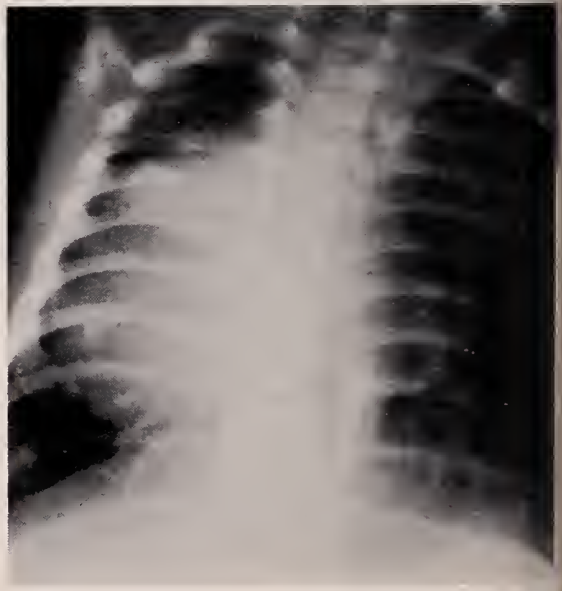

Fig. 2—Frontal view of the thoracic roentgenogr showing displacement of the heart to the right s The pulmonary vasculature is increased. The bari filled fundus of the stomach is on the left side.

This study was supported by Public Health Service Research Grant 5 RO1 HL05694 and Research Training Grant 5 TO1 HL05570 from the National Heart and Lung Institute.

*Department of Pathology, United Hospitals-Miller Division, St. Paul, Minnesota and the Departments of Pathology and Pediatrics, University of Minnesota, Minneapolis, Minnesota.

Γ" waves were inverted over the right precordial leads nd upright over the left side (Figure 1). Signs of right nd left ventricular hypertrophy were present. A thoracic entgenogram showed the heart to be in the right de of the chest (Figure 2). There was moderate car- iomegaly. The pulmonary vasculature appeared in- eased. The stomach was normally placed.

The infant died suddenly on the third hospital day.

athologic Features

The body configuration was that of *situs solitus*. The sential pathologic findings were confined to the car- ovascular system. The heart was moderately enlarged id situated in the right hemithorax. The interior of the eart showed the usual characteristics of the heart in *tus solitus* in addition to tricuspid atresia and persistent uncus arteriosus.

The right atrium was dilated and hypertrophied and ceived the superior and inferior venae cavae and the ronary sinus normally. The tricuspid valve was ab- nt, its place being represented by a dimple (Figure ı) in the floor of the right atrium. The fossa ovalis owed a short valve which resulted in a 15 x 6 mm. mmunication with the left atrium. This opening pro- ded the only exit from the right atrium.

The pulmonary veins connected normally with the ft atrium. The mitral valve was normal and continuity ith the truncus valve was present.

The left ventricle showed a normal-sized cavity but e walls were thicker than normal. A wide ventricular septal defect occupied the membranous area and the subjacent muscular tissue. This was the only avenue leading into the right ventricle. The latter chamber was a small, pouch-like structure.

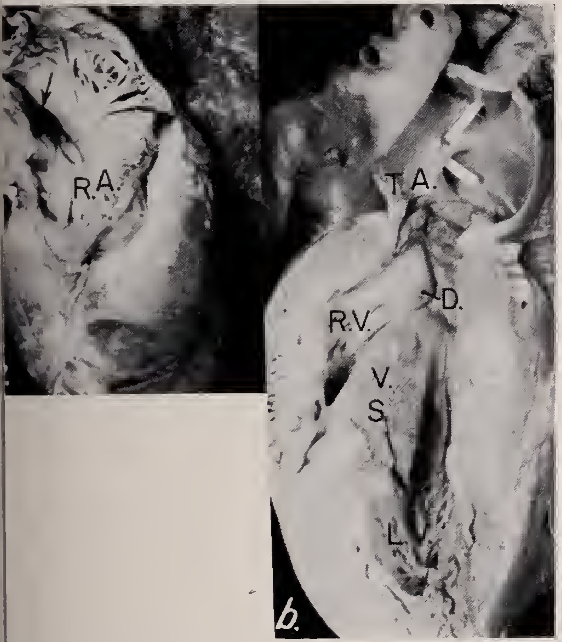

Fig. 3—*(a)* Interior of the right atrium showing tricus- l atresia and a fossa ovalis atrial septal defect (arrow).) Interior of the ventricles and the truncus arteriosus. ıe left ventricle and the right ventricle communicate ough the ventricular septal defect lying below the ıncus valve. The truncus arteriosus arises from both ntricles. The right and left pulmonary arteries (probes) se separately above the dysplastic truncus valve. . = ventricular septal defect; L.V. = left ventricle; A. = right atrium; R.V. = right ventricle; T.A. = ıncus arteriosus).

Arising above the ventricular septal defect was a single artery guarded by a dysplastic, tricuspid semilunar valve. The single vessel, which was interpreted as persistent truncus arteriosus, measured 1.2 cm. in diameter. It gave rise to the two coronary arteries. From its lateral wall 8 mm. and 14 mm. above the valve, arose the right and left pulmonary arteries, respectively, as individual branches, each measuring about 6 mm. in diameter. Beyond the origin of the pulmonary arteries, the truncus continued as the ascending aorta. The aortic arch was left-sided.

The right lung was trilobed and the left, bilobed. The entire right upper lobe was atelectatic and appeared to be the reason for displacement of the heart into the right hemithorax. The spleen was present as a single mass in the left hypochondrium. The diagrammatic portrayal of the anomalies is presented in Figure 4.

Comment

Association of mitral or tricuspid valve abnor-

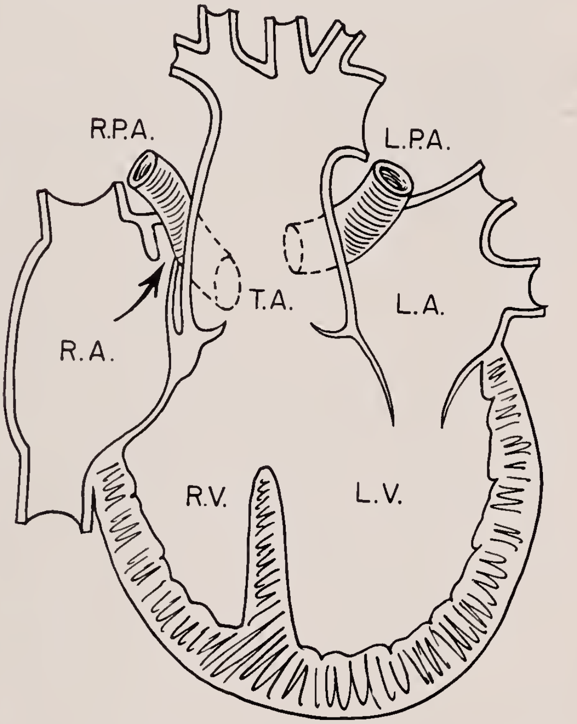

Fig. 4—Diagrammatic portrayal of the anomalies. Tricuspid atresia causes the only exit for the right atrium to be an atrial septal defect (arrow) at the fossa ovalis. The right ventricle is hypoplastic and communicates with the left ventricle through the ventricular septal defect. Mitral-truncus valve continuity is maintained. The two pulmonary arteries arise separately as in truncus arteriosus type II. (L.P.A. = left pulmonary artery; L.V. = left ventricle; R.A. = right atrium; R.P.A. = right pulmonary artery; R.V. = right ventricle).

malities in persistent truncus arteriosus is rare. Of the 80 cases of persistent truncus arteriosus reviewed by Collett and Edwards,[1] 19 had persistent common atrioventricular canal, in the remaining 61, the mitral and tricuspid valves were normal. No examples of mitral or tricuspid atresia were found. In a review of 57 specimens of persistent truncus arteriosus by Van Praagh and Van Praagh,[2] one showed persistent common atrioventricular canal and, another, congenital mitral stenosis. Abnormalities of atrioventricular valves were not mentioned by McNamara and Sommerville[3] in 27 cases of persistent truncus arteriosus studied pathologically. Atresia of the mitral valve in association with persistent truncus arteriosus and cor triloculare biatriatum was listed in one case in a review of heart disease in mongolism.[4]

In the absence of special studies in our case, one can only hypothesize concerning the hemodynamics.

The presence of tricuspid atresia results in functional cor biloculare, the left atrium providi a common mixing site and the left ventricle t main pumping source for both the systemic an pulmonary circulations.

From the anatomic state one would anticipa that there was a large volume of pulmonary flo a state supported by the roentgenogram. T cyanosis which was present resulted from intr cardiac mixing of blood and from extreme atele tasis of the right lung.

From the point of view of clinical differenti diagnosis, one anticipates that the electrocardi gram would be most helpful in establishing a dia nosis of tricuspid atresia. Changes characterist of this condition were absent in our case. One ca not explain the deviation from the usual by t presence of the associated persistent truncus a teriosus.

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Continuing Medical Education

University of Minnesota Department of Psychiatry

The Minnesota Center of the A. K. Rice Institute and the University of Minnesota Department of Conferences, Continuing Education and Extension announces the third Minnesota Group Relations Conference developed in the "Tavistock" tradition which will be held at Carleton College, Northfield, Minnesota, July 9-14, 1974. These types of conferences have attracted a large number of psychiatrists, other mental health professionals and individuals in other areas of professional and institutional responsibility since their introduction into this country in 1965 by the Department of Psychiatry, Yale University and the Washington School of Psychiatry. The Minnesota Conference, one of the more recent developments in the program of the A. K. Rice Institute, similarly has attracted a wide variety of professional and non-professional members from all parts of the country. The conferences attempt to help the members explore the nature of authority and the problems encountered in its exercise through participation in a variety of group events. In these events the members, with the assistance of qualified staff members, examine group process and the nature of authority through a combination of experiential and cognitive learning approaches. This year's conference is directed by Dr. William Hausman, Professor and Head of the Department of Psychiatry, University of Minnesota who can be contacted for more detailed information on the conference by phone (373-8869) or by mail.

Fluorescein Visualization of the Fundus

in Neurology

IRVING SHAPIRO, M.D.*; SIDNEY K. SHAPIRO, M.D.†; and GARY VAGSTAD‡

**Some of the diseases where fluorescein visualization of the fundus may be of
se in neurologic diagnosis are described. The technique of fluorescein fundus
ngiography is simple, safe, and can be of great use particularly in those entities
aving vascular or pigment abnormalities as part of the disorder.**

WITH THE USE OF an ophthalmoscope, Chao
d Flocks[1] in 1958 visualized trypan blue in the
tinal circulation of a cat. In 1961 Novotny and
lvis reported a method of photographing fluores-
nce in the circulating blood of the human
tina.[2]

Since that time there has been a voluminous
terature in ophthalmologic publications describ-
g fluorescein visualization of the fundus. There
s been, however, a dearth of publications in
e literature of other medical disciplines on this
bject. This technique can be of great value in
e diagnosis of many conditions and the purpose
this paper is to familiarize practitioners with
e diagnostic technique of fluorescein fundus
otography and underline its usefulness in the
agnosis of neurological disorders.

Technique

With the pupils dilated and the patient sitting
the retinal camera equipped with appropriate
lters, 5 cc's of 10% fluorescein is injected rap-
ly into the antecubital vein. This may be fol-
wed immediately by a 5 cc injection of saline
t this latter is not essential. Retinal photo-
aphs are taken quickly at intervals for the initial
ases of the circulation and then more delayed
otographs are taken to see if there is any un-
ual leakage or persistence of the fluorescein.
he initial serial photographs may be taken as
equently as 1/10th of a second, but ordinarily for clinical purposes this frequency of photograph is not necessary and usually the initial photographs are taken at intervals of one to two seconds. The delayed photographs are usually taken at 15 and 30 minutes.

Normal Fundus Fluorescein Appearance

In a normal fluorescein fundus photograph, the retinal blood vessels are outlined sharply by the fluorescein dye. Normal retinal blood vessels are impermeable to fluorescein. The ability to visualize the underlying choroidal circulation is determined in part by the density of the retinal pigment epithelium. If the retinal pigment epithelium is intact, choroidal fluorescence does not show. A deficiency in the retinal pigment epithelium allows choroidal fluorescence to be seen. Pathological retinal blood vessels may be permeable to fluorescein and once fluorescein is extravascular in the retina it may persist in the retina for some hours. Retinal hemorrhages and hard exudates do not absorb fluorescein and retinal hemorrhages will appear in black in the fluorescein photograph. Soft exudates do absorb fluorescein.

Figure 1 shows a normal fluorescein pattern of the fundus. In this phase of the circulation one can see the distinct white fluorescein in the retinal arterioles sharply outlined against a more generalized and less white fundus background of nonuniform contrast. The less distinct background of nonuniform white is due to the underlying choroidal circulation. In this photograph the retinal veins are still black indicating that they have no fluorescein in them, representing the

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apolis, Minnesota.

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innesota, Minneapolis, Minnesota.

arteriolar phase of the circulation. Very soon after the arteriolar phase there will be an arteriolar-venous phase in which both retinal arterioles and veins would have sharp white contrast due to the fluorescein in them. This would then be followed by a venous phase wherein the veins would be seen to be filled out with white fluorescein and the retinal arterioles, in turn, would become black.

The optic disc from which the retinal vessels originate has very little fluorescence. A pale fluorescence in the center is normal and represents, in this optic disc, a physiologic depression.

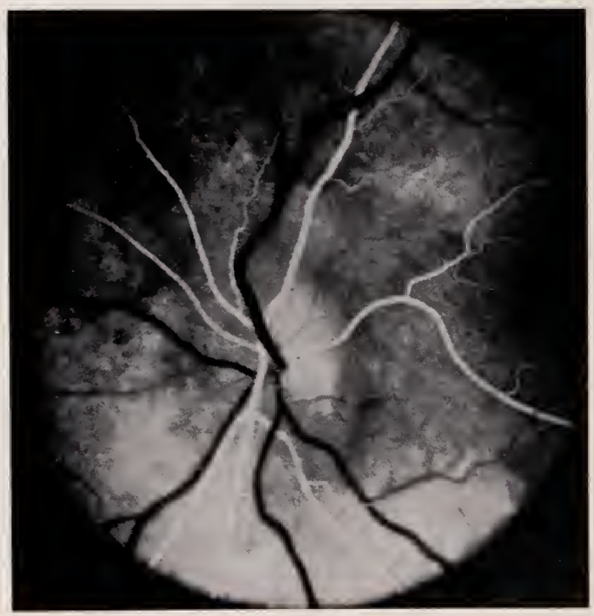

Fig. 1—Normal fluorescein pattern.

Pathologic Conditions in Which Fluorescein Fundus Photography is of Diagnostic Value

It is not within the scope of this paper to fully outline all of the conditions in which fluorescein visualization of the fundus is of diagnostic value. The Table indicates some neurologic conditions in which this technique may be of considerable value. Excluded from this discussion are primary ophthalmologic conditions which do not have neurologic features. For further information basic textbooks in ophthalmology should be consulted.[3,4]

A diagnosis can be established by direct ophthalmoscopic examination in many instances described in the Table. However, in equivocal cases, fluorescein may give diagnostic information. To underline the value of this technique, several fluorescein photographs will be demonstrated and discussed, and comments will be made on the other entities in the Table describing their fluorescein characteristics.

TABLE

A. Optic Disc
    1. Papilledema
    2. Papillitis
    3. Optic Atrophy
    4. Myelinated Nerve Fibers
    5. Drüsen
B. Retinal Diseases with Neurologic Implications
    1. Tumor
    2. Angioid Streaks
    3. Retinitis Pigmentosa
    4. Chorioretinitis e.g. toxoplasmosis
    5. Diabetic Retinopathy
C. Phakomatoses
    1. Von Hippel-Lindau Disease
    2. Sturge-Weber Syndrome
D. Circulatory Disorders
    1. Central Retinal Artery Occlusion
    2. Branch Retinal Artery Occlusion
    3. Central Retinal Vein Occlusion
    4. Partial Retinal Vein Occlusion
    5. Embolus
    6. Dysproteinemias
    7. Anemia

Optic Disc

Figure 2 shows the fluorescein appearance
early papilledema, a result of an intracrani
space-occupying lesion in a 15 year old boy. T
network of newly engorged capillaries on the di
are shown by fluorescein.

Shikano and Shimizu[4] indicate that the cardin
fluorescein findings of papilledema are dilatio
and increase in the number of visible capillari
over the disc, rapid extravasation of fluoresce
from the capillaries, and microaneurysm formation of affected capillaries over the disc area. T
earliest leakage of fluorescein is often above an
below the disc where the major blood vessels a

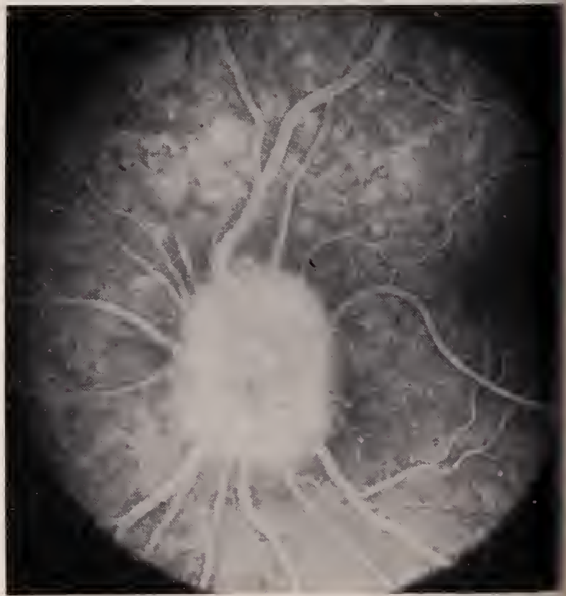

Fig. 2—Papilledema.

ocated. Fluorescein would thus be of great alue in the differentiation of true papilledema rom pseudo papilledema, as pseudo papilledema vould show none of the findings noted above.

Papillitis cannot, with certainty however, be lifferentiated from papilledema by fluorescein echnique. Shikano and Shimizu[4] feel there is inrequent microaneurysm formation in optic neuriis and papillitis, but this is not an adequate riterion for separating papillitis and papilledema.

Optic atrophy tends to show less early fluoresence than does a normal disc, but increased luorescence can be seen in the delayed photographs.[3]

Intact myelinated nerve fibers do not take up luorescein and their lack of fluorescence can be f value in their diagnosis.

Drüsen of the optic disc may appear as spots of unctate fluorescence in the early phases of cirulation but show more definite fluorescence in he late phases.

Retinal Entities with Neurologic Implications

Figure 3 is the fluorescein pattern of a maligant melanoma of the choroid. This photograph hows punctate staining with fluorescein which, in hotographs of later phases of circulation, show oalescence of the punctate staining. The puncate staining and coalescence become more marked n the late stages of the fluorescein angiogram.

Angioid streaks give a peculiar but characterisic fundus appearance wherein the streaks appear ften as slightly brownish, irregular and abnormally placed blood vessels. The streaks are due primarily to degenerative changes affecting particularly the elastic membrane of Bruch's membrane, the membrane between the retina and choroid.[5] Angioid streaks in the fundus have been associated with pseudoxanthoma elasticum, Paget's Disease, senile elastosis, Sickle cell disease, and various other systemic entities including hyperphosphatemia and some syndromes of calcinosis. There has been a recent monograph written by Paton[6] pertinent to the relationship of angioid streaks to systemic disease.

The presence of angioid streaks is not only important in helping to establish the diagnosis of systemic diseases with which it is associated, but it also has important functional significance for the eye, because macular degenerative disease and poor central vision often supervene in the presence of angioid streaks. Figure 4 shows (the fluorescein photograph) the appearance of angioid streaks in the fluorescein photograph. The retinal arteries and veins are filled with fluorescein, but in addition, there are irregular lines of fluorescent material both around the nerve head and leading towards a central retinal scar, the latter appearing as a triangular area outlined in black.

The usual finding in retinitis pigmentosa is a minute spotty pattern (on fluorescein angiography). Figure 5 is *not* the fluorescein pattern of retinitis pigmentosa, but is shown as a good example of the change of background due to retinal pigment epithelium deficiency. Ophthalmoscopic

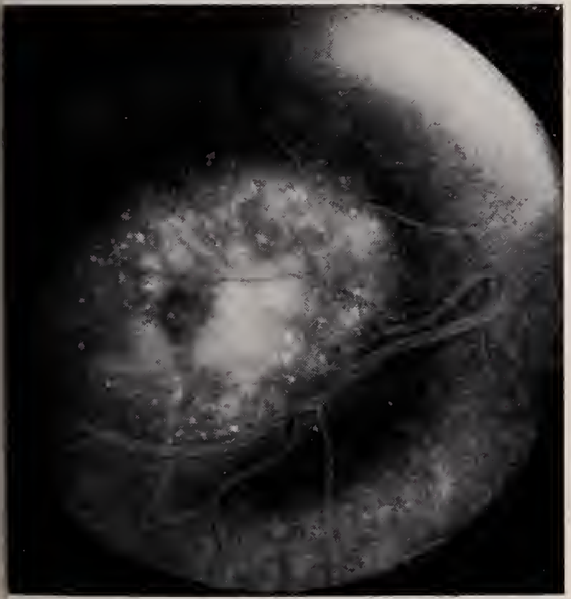

Fig. 3—Malignant melanoma.

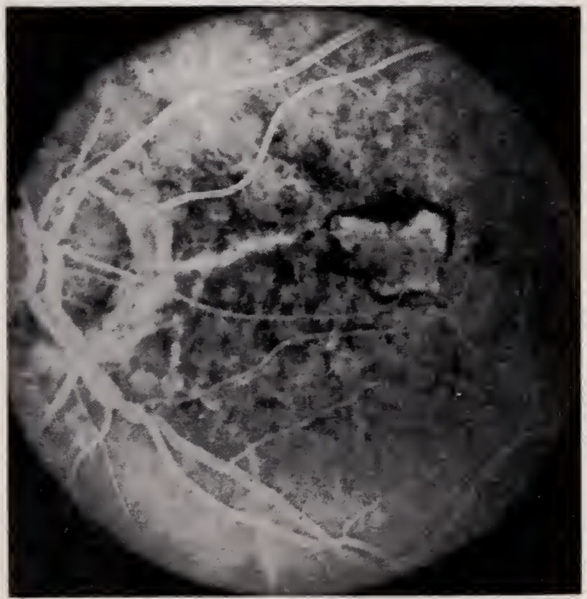

Fig. 4—Angioid streaks.

examination of this 27-year-old female indicated a fine diffuse pigmentary change of the entire retina. Visual acuity was decreased into the 20/50 line and visual fields were markedly constricted. The fluorescein photograph shows a marked increase in the choroidal background as the choroidal fluorescence is no longer screened by the deficient retinal pigment epithelium. In this photograph there can be seen fluorescence in retinal vessels in the usual linear fashion, but the outstanding feature of the photograph is the rather marked and diffuse choroidal fluorescence shown by the absence of the screening pigment epithelium. Thus, with any disorder which disturbs retinal pigment epithelium, there will be changes seen on fluorescein angiography.

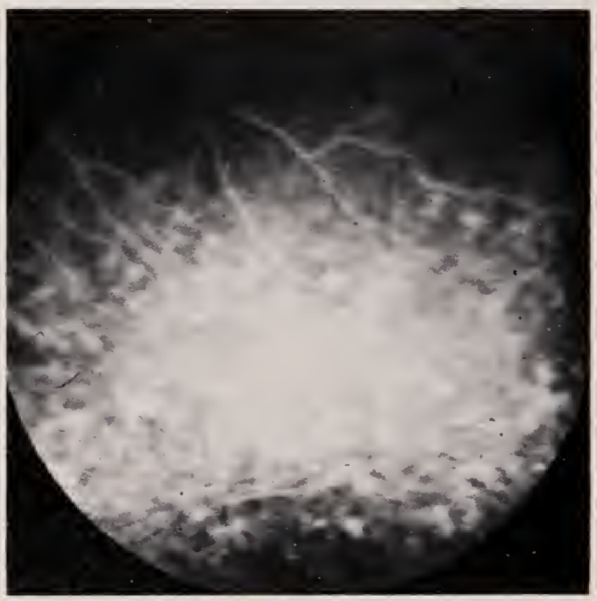

Fig. 5—Retinal pigment epithelium deficiency.

Acute chorioretinitis will often show brilliant late staining with fluorescein.

Voluminous publications pertinent to diabetic retinopathy have been published and a complete discussion of this large and important topic is not in order here. Suffice it to say that fluorescein is very useful in showing the capillary dilatation, microaneurysm formation, irregular filling of retinal vessels, closure of capillary areas, formation of shunt vessels and neovascular formations which are so much a part of diabetic retinopathy.[7]

Phakomatoses

Ophthalmoscopically, the typical retinal lesions of Von Hippel-Lindau Disease are solitary or multiple raised nodules, sometimes pink, but usually whitish-gray in color due to overlying exudate. Fluorescein photography shows rapid fil ing of the hemangioblastoma, fine neovasculariz tion on the tumor surface and transudation fluorescein from new vessels on the tumor surfa with gross leakage of fluorescein from the tum surface.[8]

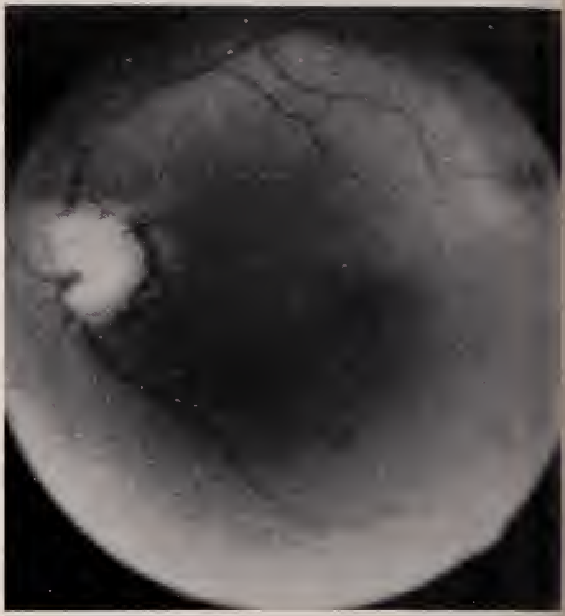

Fig. 6—Central retinal artery occlusion.

The retinal component of the Sturge-Web Syndrome is a hemangioma of the choroid. Flu rescein will show the hemangioma to be bright fluorescent very early in the circulation and have, in the late phase, patchy and mottled flu rescence.

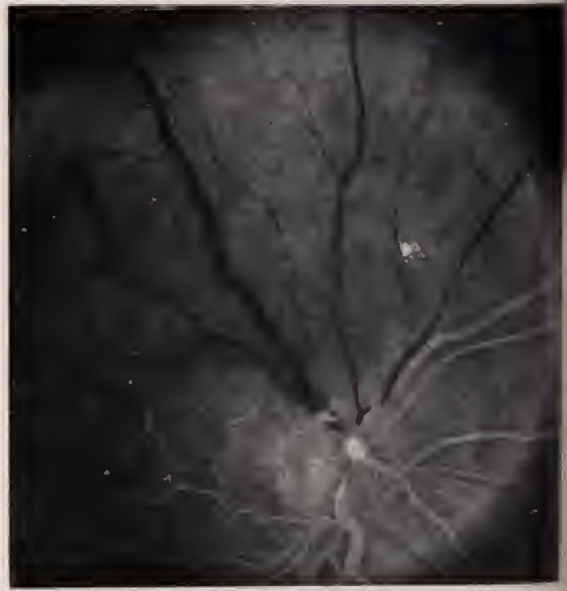

Fig. 7—Occlusion of superior temporal retinal ar rioles.

Circulatory Disorders

Figure 6 shows that fluorescein is in the eye s it is visible in the physiologic cup area of the ptic disc and can be lightly seen in one inferior mporal arteriole. The absence of fluorescein the remainder of the arterioles is indicative of a ntral retinal artery occlusion.

An occlusion of a superior temporal retinal rteriole can be seen in Figure 7, with a marked ntrast between the fluorescein seen in the patent ssels and the lack of fluorescein in the blocked ssels which appear black in the photograph. his was a 30-year-old female who had an emolic occlusion of the superior temporal retinal rteriole. In other areas of the fundus, both rterioles and veins contain blood and show the ormal whitish fluorescein appearance. Retinal mboli often arise from atheromatous plaques at e carotid bifurcation.[9]

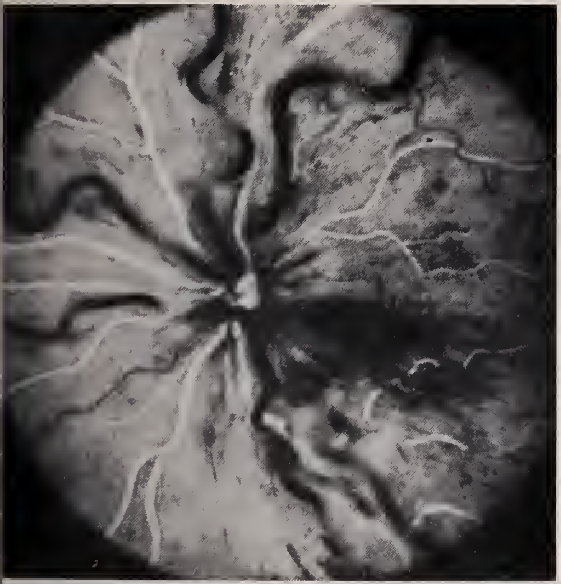

Fig. 8—Central retinal vein occlusion.

Another example of circulatory impairment is monstrated in Figure 8, which shows a central tinal vein occlusion. Here the arterioles may seen to be fluorescent and normal. The black tinal veins indicate that no significant amounts fluorescein are entering these vessels because a marked delay in filling of the engorged retinal ins. The streaks of black spread over the fundus e streaks of retinal hemorrhage which prevent e underlying normal choroidal fluorescence om being visible. A less acute stage can be en in Figure 9, representing an old partial retinal vein occlusion. In this photograph the fluorescein shows aneurysmal dilatations of many of the capillary structures below and temporal to the macula. It should be noted that the blackish avascular appearance to the macula is a normal appearance on fluorescein angiography.

Fundus fluorescein photographs of dysproteinemia and anemia can be quite useful in diagnosis of these entities. In macroglobulinemia, venous congestion, capillary dilations and microaneurysms may be seen. In anemia, retinal arterioles may be seen to be of wide caliber, and there may also be retinal hemorrhage, which as noted priorly,

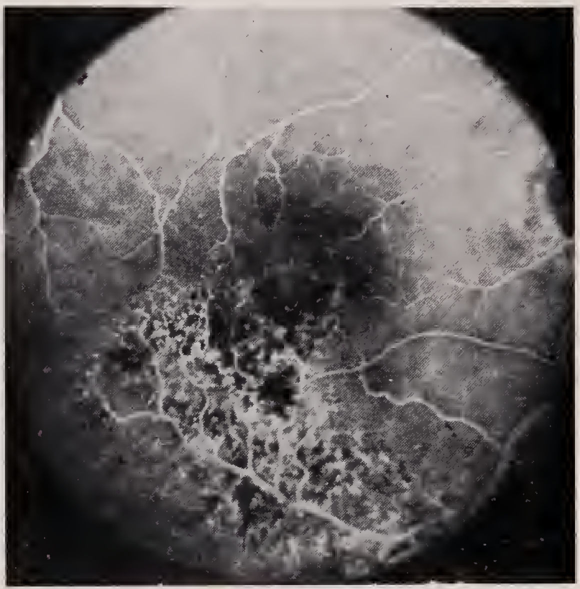

Fig. 9—Old partial retinal vein occlusion.

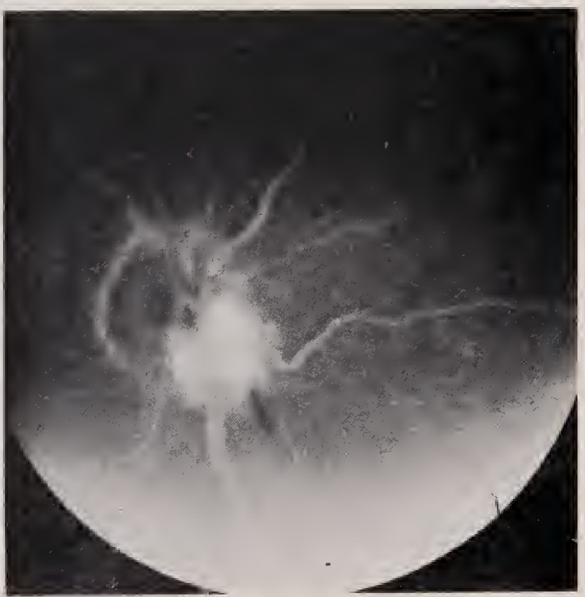

Fig. 10—Neovascular change and hemorrhage at the optic disc.

will appear black in the fluorescein photograph.

Figure 10 represents the fluorescein picture seen in a 56-year-old man who had neovascularization of a portion of the optic disc (nerve head) associated with a streak hemorrhage. The underlying disease was probably an arteritis. The neovascularization shows as a fluffy, whitish area and the streak hemorrhage as black.

Toxicity of Intravenous Fluorescein

Fluorescein angiography of the optic fundus has little toxic effect. Probably the most common side effect is nausea, in one series occurring in 15% of 680 diabetic patients.[10] There have been large numbers of fluorescein angiograms (angiographies) done and few serious complications have been reported. Stein and Parker[11] collected 55 cases of reaction to intravenous fluorescein. The majority of the reactions (67.3%) were of the allergic type and most of these were characterized by urticaria only. About 29% of these allergic reactions were of a severe nature and 11 presente a shock-like picture. In most cases recovery wa uneventful, but one patient developed a myoca dial infarction several hours after the procedu and died. Thus, even though fluorescein angiog raphy is relatively very safe and is most certainl an office procedure, preparations to handle th occasional severe allergic reaction should be mad

As fluorescein angiography is often done i diabetics, it is important to note that within a hour following intravenous administration of th fluorescein, a routine urinalysis will indicate pro tein and be positive for reducing substances. Th latter effect may persist for four to five days an the patient should be warned not to be concerne about this.[12]

The patient should also be warned that the ski is stained yellow for two to four hours after th injection and that the urine may be fluorescen for 24 to 36 hours, but that neither of thes things are of significance or of permanence.

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Headwaters Clinical Conference

The Third Annual Headwaters Clinical Conference has been scheduled for Friday, June 21, 1974, at Ruttger's Birchmont Lodge in Bemidji, Minnesota. The theme for the discussion will be "Pediatric Medical/Surgical Problems in General Practice." For detailed information and advance registration cards contact Headwaters Clinical Conference Committee, Bemidji Hospital, Bemidji, Minn. 56601.

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*Why are the Whigs and the Tories like scarlet fever and the measles?—Because there's no telling which is the worse.**

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*"A Bitter Draught:" Punch, 1841.

Intestinal Obstruction by A Watermelon Seed

FREDERIC W. GRANNIS, M.D.* AND RAYMOND A. LEE, M.D.*

Watermelon seed and a fecalith produced intermittent occlusion of the narrowed men resulting in increasingly severe intermittent relapsing bowel obstruction in a tient with strictured anastomosis.

A PATHOLOGIC LESION may sometimes oc- sion such a serious strain on physiologic com- nsatory mechanisms that a relatively innocuous ded stress may suffice to cause serious sympto- atic illness. The following case demonstrates is principle.

Case Report

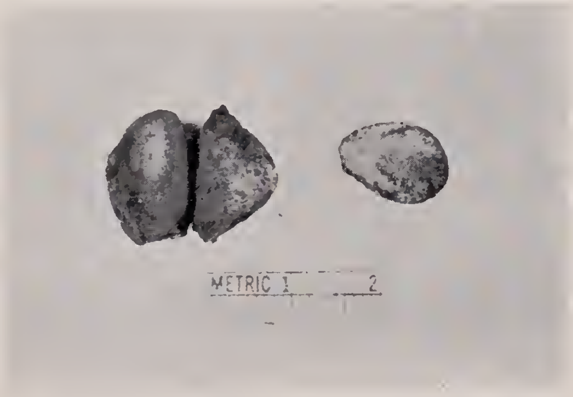
A 40-year-old woman returned to the Mayo Clinic er an interval of 31 years for evaluation of recurring dominal pain, distention, and vomiting of two years' ration. In 1940 the patient had a catastrophic illness rting with a ruptured appendix with peritonitis, mul- le intra-abdominal abscesses, and enterocutaneous and terovesicular fistulas. During this period she under- nt six operations. She was first seen at the Mayo inic in 1942. Exploratory laparotomy revealed multiple tulas in the small bowel, of the skin, and in the nary bladder. A 40-cm segment of terminal ileum s resected and continuity was restored by side-to-side o-ascending colostomy by a closed method.

The patient did well over the intervening years until 67 when she began to have diarrhea (three to 15 ols per day) and lost 20 pounds. In 1971 she began experience increasingly severe and frequent episodes bloating, severe cramping abdominal pain, nausea, d vomiting. Between attacks she noted almost daily dominal discomfort and audible peristalsis. In Jan- y 1973 she was hospitalized elsewhere for so-called estinal obstruction. At this time she was told that she o had a pelvic mass and surgery was advised. Be- use of her childhood experience she was resistant to gery, but in 1973, because of the increasing severity her symptoms, she returned to the Mayo Clinic for aluation of these two problems.

Physical examination was unremarkable except for tention of the lower part of the abdomen and a large t cystic mass in the pelvis. Results of all laboratory ts were within normal range. An excretory urogram owed a large pelvic mass indenting the bladder and placing the ureters laterally.

On June 15, 1973, exploratory laparotomy was performed through a lower midline incision. A large cystic mass was noted filling the pelvis and extending up to the level of the umbilicus. A total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. Attention was then directed to the intestines. Surprisingly, few filmy adhesions were found and the small bowel and colon appeared to be normal in every way. Two small, hard masses were detected lying intraluminally in the terminal portion of the small bowel. We were unable to pass these bodies through the ileocolostomy at the site of the anastomosis done 31 years previously. The terminal portion of the ileum was opened accordingly and two small masses considered to be fecaliths were removed. The ileum ended in what, at first, seemed to be a complete cul-de-sac, but we finally were able to pass a small curved clamp through a tiny aperture, not more than 1 or 2 mm wide, and into the colon. The septum between ileum and colon was incised creating an anastomosis of generous size and the enterotomy was repaired.

The patient's postoperative course was uneventful and she was dismissed from the hospital on the 13th day after the operation. The pathologist reported a left tubo-ovarian cyst measuring 18 by 15 by 12 cm and weighing 2,200 g. The bodies removed from the terminal part of the ileum were a fecalith (2 by 1.5 by 1 cm) and a watermelon seed (1.2 by 0.9 by 0.3 cm) (Figure 1). On questioning, the patient remembered that she had last



Figure—Watermelon seed and fecalith removed from terminal portion of ileum.

Department of Surgery, Mayo Clinic and Mayo Foundation, chester, Minnesota.
Reprint address: Dr. F. W. Grannis, c/o Section of Publications, yo Clinic, 200 First Street SW, Rochester, MN 55901.

eaten watermelon two years previously, but that it had given her "so much trouble" that she had not eaten it again. It seems probable to us that the anastomosis had strictured many years before and that she was functioning reasonably well until two small intraluminal bodies, a fecalith and the watermelon seed, began t produce intermittent occlusion of the narrowed lume with a resulting clinical picture of increasingly seve intermittent relapsing bowel obstruction.

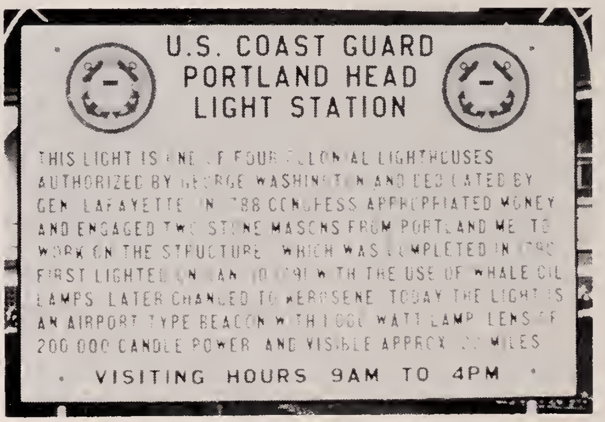
Cover Photo

"Portland Head Light"

Dr. Rodger R. Lundblad, Minneapolis urologist and President of the Twin City Urological Society, took the cover photo while on vacation in Maine with his family in the summer of 1971. He used a Nikkormat FTN with a 50 mm lens and Kodachrome II film.

The Portland Head Light guards the harbor at Portland, Maine, and below is photo of the plaque which carries the history of this famous landmark.

Dr. Lundblad is an accomplished photographer and has been named as one of the winners of the best cover award for 1974 by the Board of Editors of Minnesota Medicine.



U.S. COAST GUARD
PORTLAND HEAD
LIGHT STATION

THIS LIGHT IS ONE OF FOUR COLONIAL LIGHTHOUSES AUTHORIZED BY GEORGE WASHINGTON AND DEDICATED BY GEN LAFAYETTE IN 1788 CONGRESS APPROPRIATED MONEY AND ENGAGED TWO STONE MASONS FROM PORTLAND ME TO WORK ON THE STRUCTURE WHICH WAS COMPLETED IN 1790 FIRST LIGHTED ON JAN 10 1791 WITH THE USE OF WHALE OIL LAMPS LATER CHANGED TO KEROSENE TODAY THE LIGHT IS AN AIRPORT TYPE BEACON WITH 1000 WATT LAMP LENS OF 200 000 CANDLE POWER AND VISIBLE APPROX [illegible] MILES

• VISITING HOURS 9AM TO 4PM •

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Partial Anomalous Pulmonary Venous Drainage—Helseth and Peterson (Page 463)

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Partial Anomalous Pulmonary Venous Drainage, Intact Atrial Septum and Acquired Mitral Stenosis

Surgical Correction

HOVALD K. HELSETH, M.D.* AND CHARLES R. PETERSON, M.D.*

When anomalous pulmonary venous drainage of the right upper and middle bes to the superior vena cava is associated with mitral stenosis and intact atrial eptum the diagnosis will be aided by observing differences in pulmonary artery edge pressures, by selective right and left pulmonary artery dye dilution curves, nd by the utilization of selective pulmonary angiography.

In this case the creation of a large atrial septal defect allowed replacement of e mitral valve through the right atrium. A pericardial baffle was fashioned to eturn the anomalous pulmonary venous drainage to the left atrium and to form n interatrial septum.

An accurate preoperative diagnosis facilitated this total anatomic correction.

MITRAL STENOSIS combined with an anomalus pulmonary venous connection is infrequent. he difficulties and the importance of accurate reoperative cardiac catheterization diagnosis ave been emphasized, as have the problems of incomplete surgical correction. Total anatomic corection of this combination has been reported only hen mitral stenosis was combined with anomlous venous drainage from the left lung. Reorted cases of mitral stenosis combined with an nomalous venous connection of the right lung to e superior vena cava have been incompletely orrected and with unsatisfactory results. This ariant has been handled by commissurotomy, ith or without pulmonary lobar artery and vein gation, pulmonary resection, or an attempt to nastomose the anomalous right pulmonary vein irectly to the left atrium. To our knowledge a omplete intracardiac correction has not been escribed.

This report concerns a patient with rheumatic itral stenosis and associated right upper and iddle lobe venous drainage to the superior vena

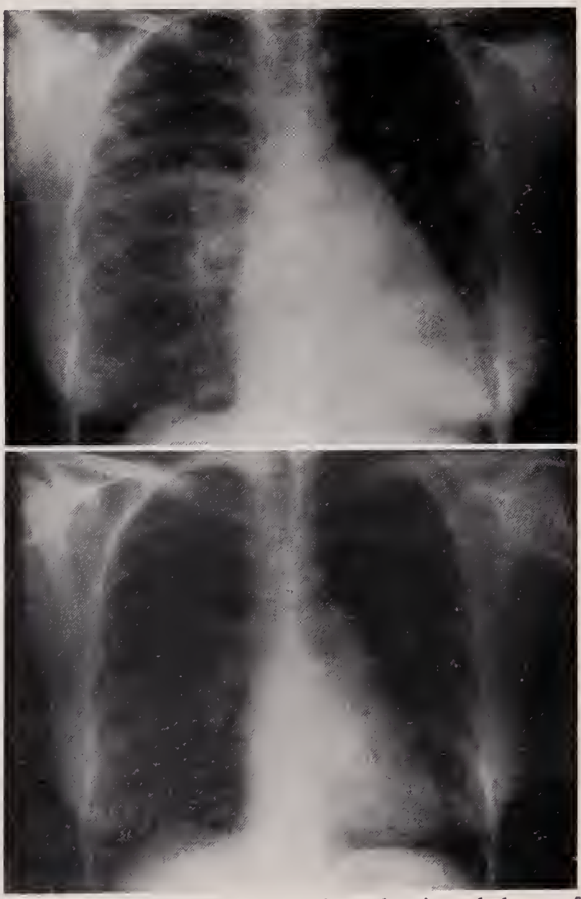

Fig. 1—(top) Preoperative Xray showing plethora of right lung field and cardiomegaly, (bottom) Postoperative Xray.

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cava with an intact atrial septum. Important aspects of the cardiac catheterization and an anatomic method of repair are presented.

Case Report

A 43-year-old woman was referred for evaluation of dyspnea and fatigue. The history included rheumatic fever at age 12 and a staphylococcal groin infection at age 33 with possible myocarditis. A murmur was heard during her third pregnancy but, save for easy fatigability, she did well until the onset of increasing dyspnea one year prior to admission. She progressed to NYHA class 3-4 and spent four weeks in bed prior to hospital evaluation.

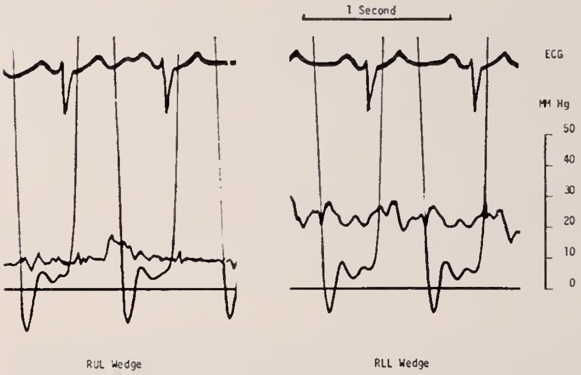

Fig. 2—Differences in pulmonary artery wedge pressures observed in the right upper lobe and right lower lobe.

On admission the blood pressure was 110/70 mm Hg and the pulse was 80 and regular. There was cardiomegaly with a prominent right ventricular heave. A grade 3/6 systolic ejection murmur and a grade 2/6 diastolic murmur were heard loudest at the upper left sternal border and the apex, respectively. The electrocardiogram showed marked right axis deviation and p-mitrale. The chest roentgenogram showed prominent pulmonary vasculature, cardiomegaly, and mild left atrial enlargement (Figure 1a). The clinical impression was atrial septal defect and probable mitral valve stenosis.

Preoperative Cardiac Catheterization

Cardiac catheterization was performed on September 21, 1972. The results are summarized in the Table. On passage of the venous catheter from the right arm, the tip was seen to enter the right mid-lung field from the superior vena cava. Blood sampling from the suspected anomalous pulmonary vein showed an oxygen saturation of 96%. There was an oxygen step-up in the superior vena cava and the high right atrium. Pulmonary artery wedge pressure in the right upper lobe was normal and similar to the right atrial pressure, whereas the wedge pressure was markedly elevated in the right lower lobe and the left lung (Figure 2). Cardio-green dye dilution curves showed a left to right shunt from the right pulmonary artery but none from the left, indicating anomalous right pulmonary venous drainage with an intact atrial septum (Figure 3a). Pulmonary angiography demonstrated excessive flow through the area of anomalous venous drainage in the right lung (Figure 4a). The cal-

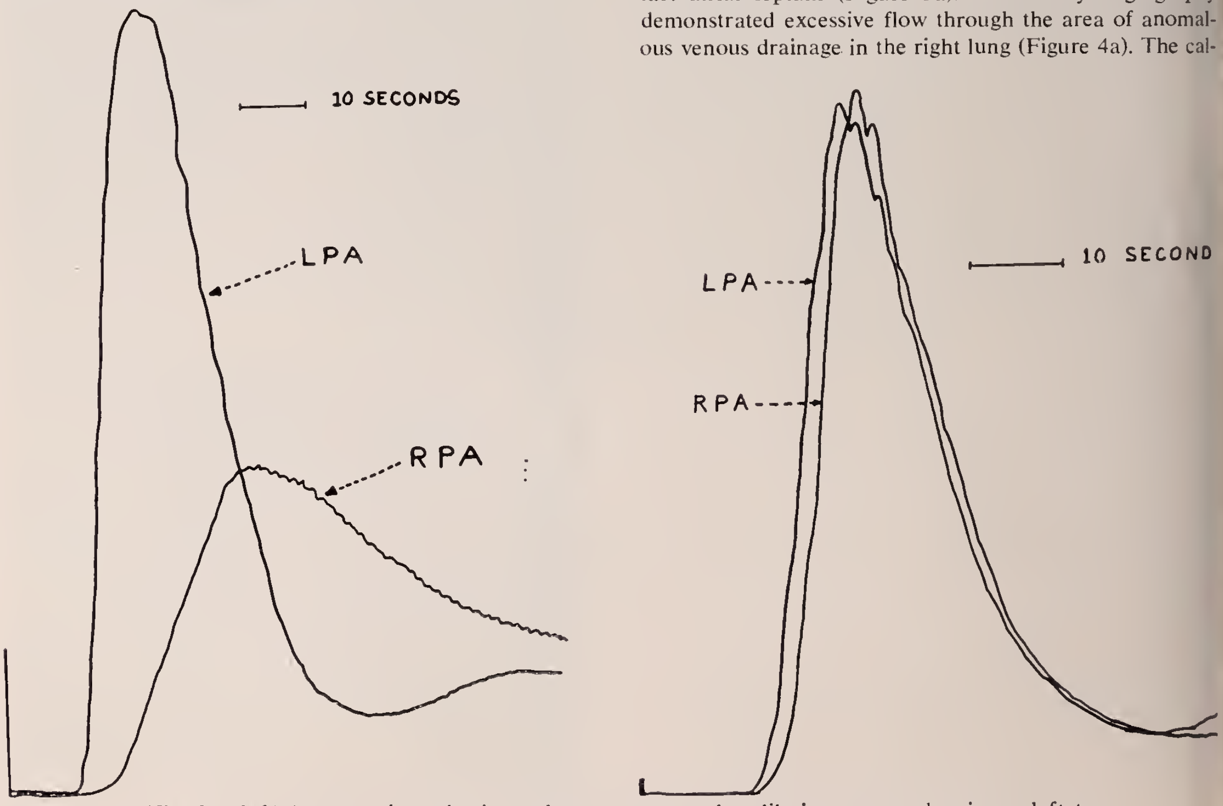

Fig. 3—(left) Preoperative selective pulmonary artery dye dilution curves showing a left to right shunt from the right pulmonary artery. (right) Postoperative dye dilution curves showing absence of a shunt.

lated left to right shunt was 65% and the calcified itral valve area was 0.9 sq cm.

perative Procedure

In October the patient underwent cardiac surgery as ustrated in Figure 5. The anomalous right upper and iddle lobe veins entered the superior vena cava four ntimeters above the superior vena cava-right atrial junction. The superior cava was twilled above the anomalous veins and the right atrium opened extending the incision up the superior vena cava. The atrial septum was intact and a large area of the superior atrial septum was excised. The stenotic mitral valve was excised through the atrial septal defect and replaced with a 3-M Starr-Edwards prosthesis. Pericardium was used to baffle the anomalous pulmonary venous drainage to the

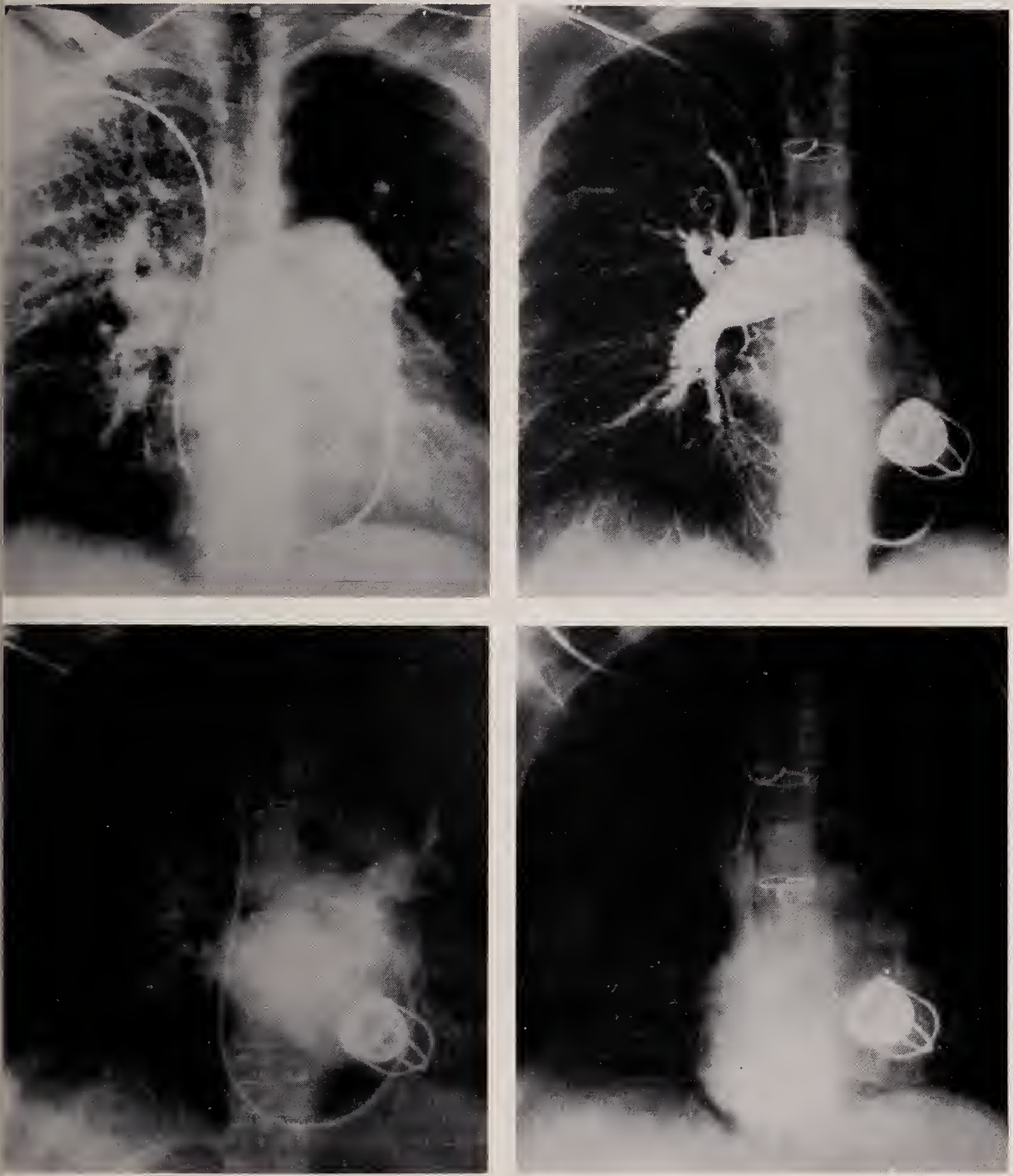

Fig. 4—(top-left) Preoperative pulmonary angiogram with increased contrast to right upper lung. (top-right) Postoperative angiogram with normal arterial distribution to the right lung. (bottom-left) Venous phase with normal drainage and separation of atria. (bottom-right) Superior vena-cavagram with no obstruction and separation of atria.

left atrium to include closure of the created atrial septal defect. The right atrial closure included a gusset of pericardium at the superior vena cava-right atrial junction to overcome superior vena caval obstruction. The postoperative course was uneventful and the patient was discharged on the eighth day.

Postoperative Cardiac Catheterization

Four months following surgery repeat cardiac catheterization was performed. At that time the patient was functional NYHA class 1-2. The chest roentgenogram showed reduction in pulmonary congestion and heart size (Figure 1b). Right heart catheterization results are summarized in the Table and show normal resting right heart pressures with no detectable left to right shunt by multiple dye curves (Figure 3b). Angiography demonstrated normal pulmonary arterial (Figure 4b) and venous distribution in the right lung (Figure 4c). A superior vena cavogram showed no obstruction in the area of the pericardial baffle (Figure 4d).

Discussion

Because of the infrequent association of anomalous pulmonary venous drainage and mitral stenosis, clinical and cardiac catheterization diagnosis may be difficult. In one group of 934 patients catheterized for mitral valve disease, some form of anomalous venous drainage was found in only four patients.[1] If, as in this report, the catheter passes into the anomalous vein the diagnosis is greatly facilitated. Several aspects of cardiac

TABLE
Cardiac Catheterization Summary

Site	Pre-Operative		Post-Operative	
	mm Hg	% 0_2 Sat	mm Hg	% 0_2 Sat
SVC		72		68
RA mean	5	86	4	69
RV	60/0-9	88	30/0-4	68
PA mean	36	90	18	68
PAW mean RUL	6		10	
RLL	24		10	
LV	125/0-7	96		
C.I.	2.6 L/M^2		2.6 L/M^2	
% Shunt Left to Right	65%		0%	

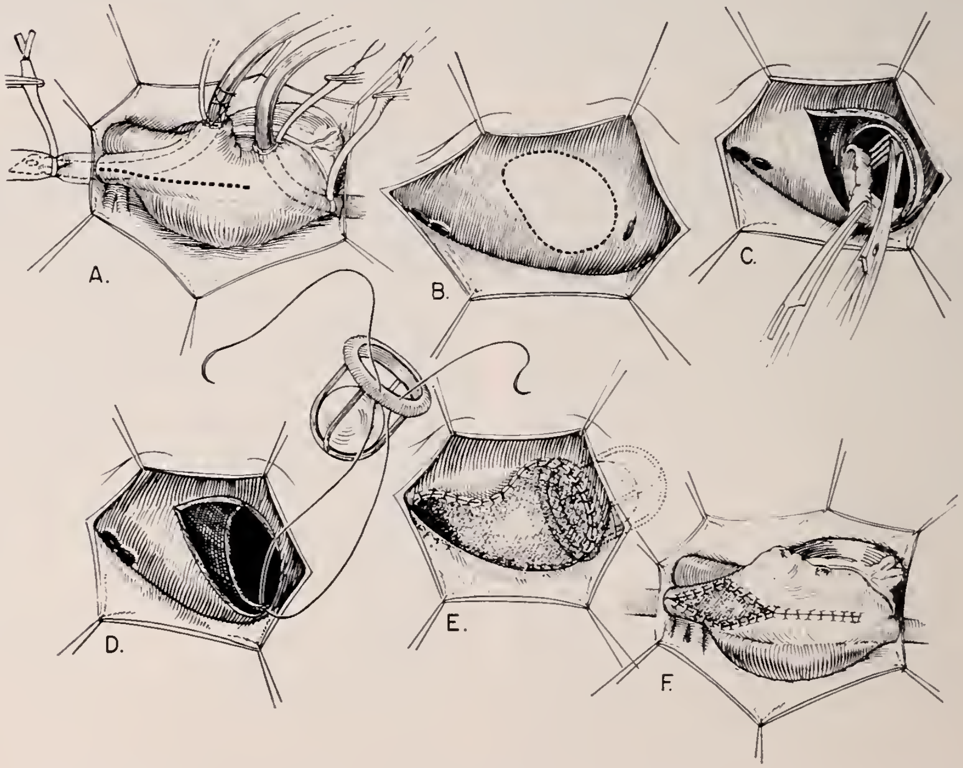

Fig. 5—(a) Right atrium opened extending incision up the superior vena cava. (b) Atrial septum excised. (c,d) Mitral valve excised and replaced through the atrial septum. (e) Pericardial baffle diverts anomalous drainage to the left atrium. (f) Right atrial closure with pericardial gusset preventing superior vena cava obstruction at the baffle site.

atheterization should be emphasized. Different ulmonary artery wedge pressures obtained from ifferent areas of the lung lead to a suspicion of nomalous pulmonary venous connection with inct atrial septum. The elevated pressures reflect ie obstructed left atrium and the more normal ressure reflects the more compliant and unobtructed right heart.[1-3] This may not always be ue as similar wedge pressures have been decribed in both normal and abnormal portions of ie lung, similar to what one would expect with ombined mitral stenosis and atrial septal dect.[4,5] Some authors have recorded a relatively ormal distribution of blood flow to both normal nd abnormal drainage areas of the lung.[4,6,7] This ick of a "safety valve" mechanism would be resent if there were an increase in pulmonary rterial resistance in the anomalous area secndary to increased flow. Mitral stenosis has been iown to decrease pulmonary vascular resistance s a result of pulmonary venous distention.[7] Toether these could contribute to equalization of lood flow. In one patient lung biopsy failed to eveal pulmonary vascular changes secondary to icreased blood flow.[4] In our patient lung biopes were not obtained, but pulmonary artery edge pressures correctly indicated the abnorality.

Of more diagnostic significance are the differntial right and left pulmonary artery dye dilution urves which will separate partial anomalous pulionary venous drainage with intact atrial septum om atrial septal defect.[5,6] Selective pulmonary ngiography can be helpful in defining which lobes rain anomalously.

Several patients with combined mitral stenosis nd partial anomalous venous drainage have not ad surgery, or have had surgery on the mitral alve alone.[1,6-8] It has been suggested that only ie mitral stenosis be repaired.[1] In patients with itact atrial septum and anomalous venous drainge, but without mitral valve disease, the majority ill have a significant left to right shunt. In one patient with anomalous right upper and middle lobe venous drainage to the superior vena cava, the left to right shunt measured 48%.[10] In our case, with the addition of mitral stenosis, the shunt was 65%. It would seem preferable to eliminate the shunt, since both mitral commissurotomy and prosthetic valve replacement will be associated with some residual left atrial pressure elevation on exercise.

Attempts to eliminate the shunt by other than anatomic methods, that is by pulmonary artery and vein ligation or by pulmonary resection, have given unsatisfactory results.[1,5] Zion was first to report a patient with mitral stenosis and anomalous left pulmonary venous drainage who underwent mitral commissurotomy alone with some improvement.[9] Successful total correction of this condition was first reported by Nichols in 1956,[11] and also by Adler,[6] and Singh.[4] These cases involved mitral stenosis and anomalous left pulmonary venous drainage to the innominate vein. They combined closed mitral commissurotomy with anastomosis of the anomalous left pulmonary vein to the left atrial appendage, a technique described by Kirklin.[12]

Several methods of correcting isolated anomalous right pulmonary venous drainage have been utilized.[8,10,12,13] When combined with mitral stenosis, these have at times been abandoned in favor of pulmonary resection or vessel ligation, which are not anatomic and which carry high morbidity and mortality rates.[1,5,14]

It would seem appropriate to combine the best corrective operation for both conditions. The mitral obstruction can be relieved and the anomalous right pulmonary venous drainage anatomically rerouted to the left atrium after creating an atrial septal defect. This procedure was followed in our patient with an excellent clinical recovery. It was done with low morbidity and with apparent anatomic correction as shown by repeat cardiac catheterization.

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8-14. Will be found on page page 458.

FEATURE SPECIAL

Historic Hospitals

Financing the Maristan of Qalaun

Entrance to Sultan Qalaun's hospital. The iron grill above the entrance is of twelfth-century French workmanship and is believed to have been captured from the Europeans in the Crusades. (Courtesy K.A.C. Creswell and Clarendon Press, Oxford.)

The maristans or hospitals of the medieval Arabs were the largest, most elaborate, and therefore the most expensive of their time. Most conspicuous of all was the hospital of the Sultan Qalaun, built at Cairo in 1284 A.D.

Since there was no charge to patients for hospitalization or medical care, the entire cost of operation had to be borne by one or more patrons, in this case the sultan himself. At the hospital's dedication Qalaun announced the institution's purpose as the care of all sick subjects, great and small, free and slave, male and female. To provide the funds for such an undertaking he simultaneously announced his endowment of the hospital with properties including market places, shops, tenements, hostelries, and lands, some as far away as Syria. The endowment, called by the Arabs a *waqf,* provided an annual income of one million dirhems and made of the hospital a permanent, free-standing institution whose title to the independently held properties was recognized by the courts.

The governor of the hospital was usually a prince or a general appointed by the sultan. The actual director, the *mutawalli,* was a physician. Assisting him were two lay officers. the *qawam* (administrator) and the *mushrif* (superintendent). The sultan's advisors managed the endowment properties; although in smaller Arab hospitals they were usually overseen directly by the administrator.

Warren L. Kump, M.D.
Minneapolis, Mn.

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An Unusual Fracture of the Sacrum

ANTHONY H. WOODWARD, M.D.* and PATRICK J. KELLY, M.D.*

Unusual fracture of the sacrum is described in an 18-year-old student.

FRACTURES OF THE SACRUM are relatively rare injuries. We recently treated a patient who had an unusual type.

Report of Case

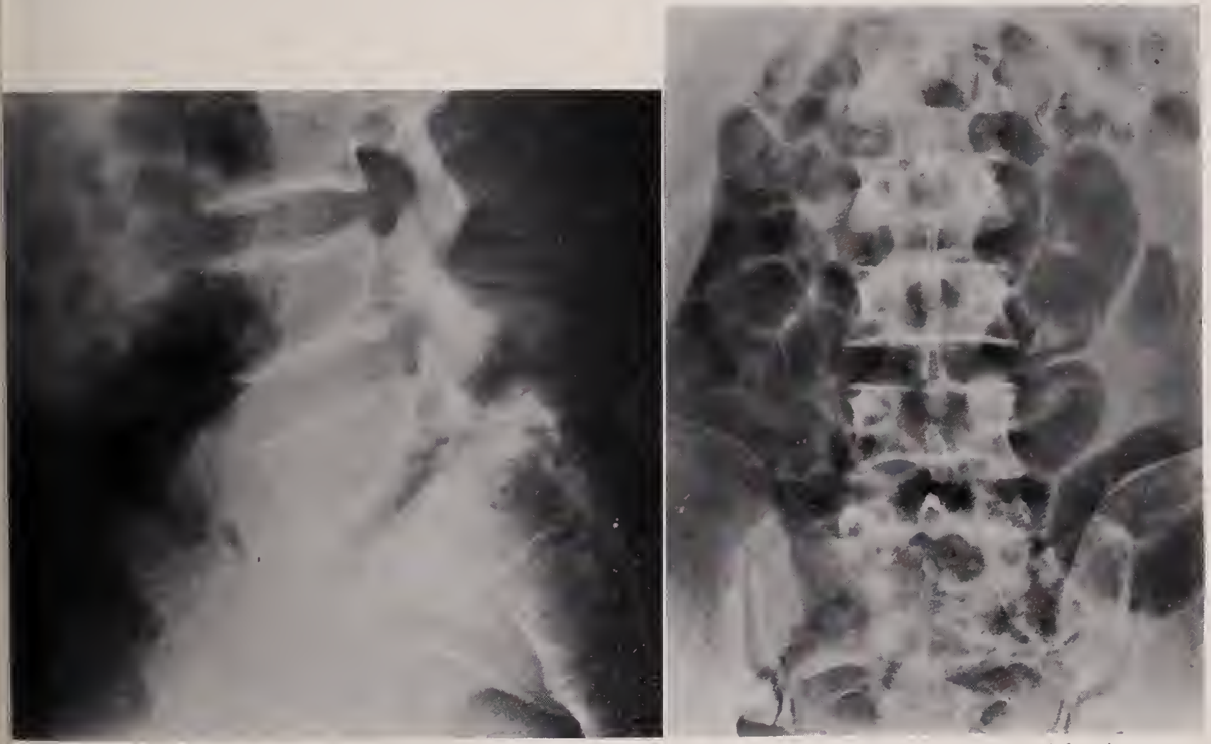
An 18-year-old student was brought to the Mayo Clinic about three hours after he had been involved in an automobile accident. He had been found lying at the side of the road, apparently having been thrown from his car. His back was covered with abrasions, and he complained of severe pain over the lumbar and sacral areas. His bony injuries were fractures of the left 10th, 11th, and 12th ribs, fractures of the transverse processes of the first, second, and third lumbar vertebrae, fracture of the right pedicle of the fifth lumbar vertebra, and fracture of the sacrum (Figure). He had weakness but not complete paralysis of the tibialis anterior, extensor hallucis longus, tibialis posterior, and peroneal muscles of the left leg. He was in profound shock and showed signs of intra-abdominal bleeding.

An emergency splenectomy was performed and a long tear in the serosa of the colon was repaired. During the abdominal exploration, a large retroperitoneal hematoma was seen on the left side. The patient made a satisfactory recovery from his skin and abdominal injuries but there was no change in the strength of his leg muscles. Three weeks after his injury, an electromyographic examination showed denervation of these muscles as well as of the lower lumbar paraspinal muscles, confirming a fifth lumbar nerve root lesion.

After three weeks of bed rest, the patient was fitted with a lumbosacral corset and he started walking with no change in his muscle weakness. Three months later he had no pain and was able to return to work, although there was as yet no increase in muscle strength.

Discussion

Fractures of the sacrum without fracture of the pelvis are uncommon. According to Rowell,[1] of 25,360 fractures at the Institute Orthopedica in Bologna, only 14 were isolated fractures of



Figure—*Left,* Lateral view of sacrum, showing anterior displacement of first sacral segment. *Right,* Anteroposterior view of sacrum, showing fracture line passing through lateral masses.

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*Department of Orthopedics, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Address reprint requests to: Dr. A. H. Woodward, c/o Section of Publications, Mayo Clinic, 200 First Street SW, Rochester, MN 55901.

See editorial, page 478.

the sacrum, and Ghilardi and Ettore[2] reported six sacral fractures in a collection of 7,000 fractures. Transverse fractures generally involve the lower three sacral segments, and displacement is unusual. Vertical fractures of the sacrum through the first and second sacral foramina have been found associated with other breaks in the pelvic ring.[3] Midline vertical fractures also have been described.[4]

Our patient sustained a form of traumatic spondylolisthesis with forward slipping of the first sacral segment. The line of separation passed through the intervertebral disk and then inferiorly through the lateral masses parallel to the sacroiliac joint. A similar injury was reported by Purser[5] in a 19-year-old girl who sustained an anterior displacement of the first sacral segment. Both patients received a severe blow to the back superior to the level of the sacral fracture. In our case, no attempt was made to reduce th displacement. We thought the weakness of th leg muscles to be due to injury of the fifth lumba nerve root and not related to the sacral fractur Purser treated his patient with Pugh's tractio for 8 weeks and apparently decreased the amou of displacement.

This type of fracture can only occur befo the sacral segments fuse and the intervertebr disks are obliterated. Fusion is said to begi across the most caudal disks at about 15 yea and progress rostrally with the first and secon sacral segments being fused by age 25.[6] Howeve Francis[7] examined a number of adolescent pelv and found that the first and second sacral se ments were frequently fused by age 18. Th unusual fracture of the sacrum would be expecte only in adolescents and young adults (less tha 25 years of age) subjected to a severe blow to th back.

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Early in the Regency of George the Magnificent, there lived in a small town in the west of England, called Clavering, a gentleman whose name was Pendennis. There were those alive who remembered having seen his name painted on a board, which was surmounted by a gilt pestle and mortar over the door of a very humble little shop in the city of Bath, where Mr. Pendennis exercised the profession of apothecary and surgeon; and where he not only attended gentlemen in their sick-rooms, and ladies at the most interesting periods of their lives, but would condescend to sell a brown-paper plaster to a farmer's wife across the counter— or to vend tooth-brushes, hair-powder, and London perfumery.*

---

*Thackeray: Pendennis, Chapter II. 1850.

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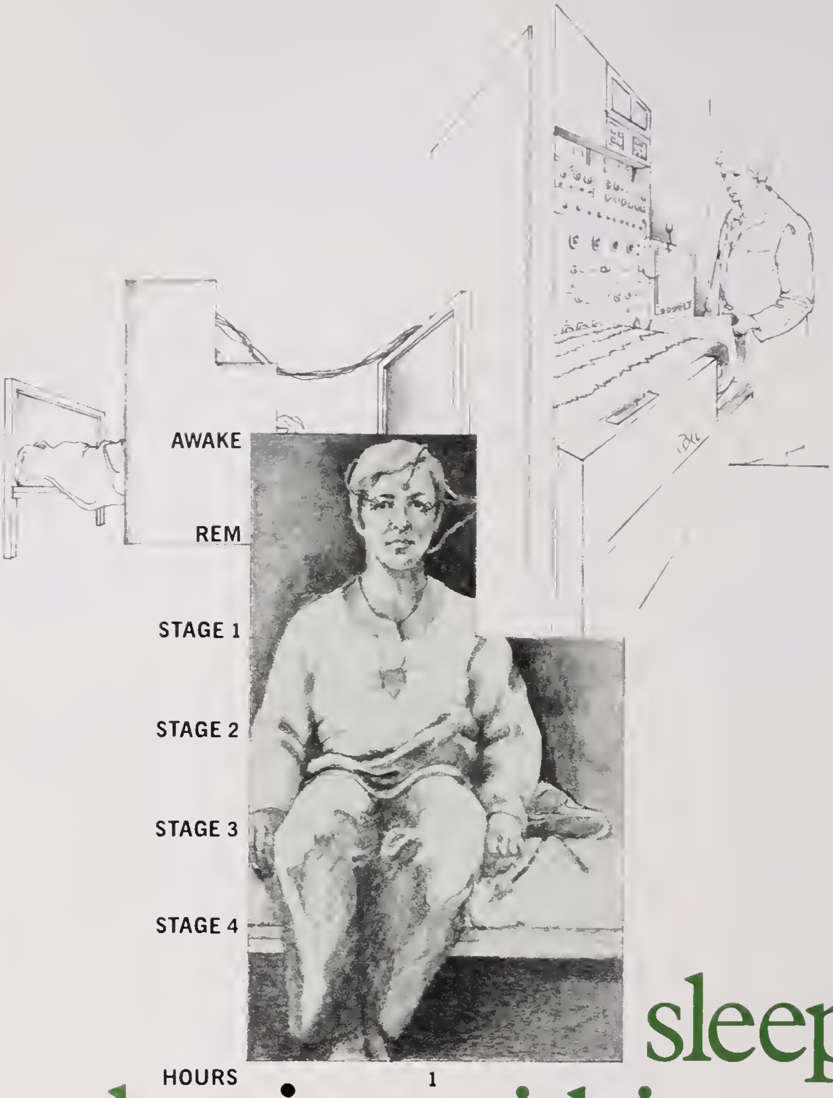

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proved by a 22-night clinical study of insomnia patients in the sleep research laboratory and at home[1]

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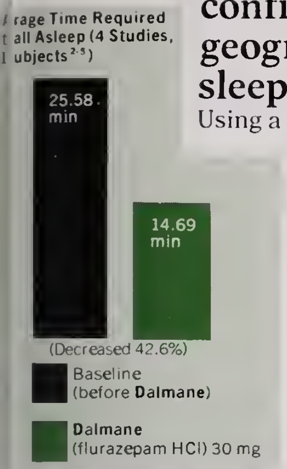

confirmed by clinical studies in four geographically separated sleep research laboratories[2-5]

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nane is generally well tolerated; morning "hang-over" has been relatively
equent. While dizziness, drowsiness, lightheadedness and the like have
noted most often, particularly in the elderly and debilitated, physicians
ild be aware of the possibility of more serious reactions, as noted below.

re prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, nmary of which follows:

ations: Effective in all types of insomnia characterized by difficulty in falling asleep, ient nocturnal awakenings and/or early morning awakening; in patients with recurring nnia or poor sleeping habits; and in acute or chronic medical situations requiring restful Since insomnia is often transient and intermittent, prolonged administration is generally ecessary or recommended.

raindications: Known hypersensitivity to flurazepam HCl.

ings: Caution patients about possible combined effects with alcohol and other CNS essants. Caution against hazardous occupations requiring complete mental alertness operating machinery, driving). Use in women who are or may become pregnant only when ntial benefits have been weighed against possible hazards. Not recommended for use in ns under 15 years of age. Though physical and psychological dependence have not been ted on recommended doses, use caution in administering to tion-prone individuals or those who might increase dosage.

utions: In elderly and debilitated, initial dosage should be ed to 15 mg to preclude oversedation, dizziness and/or ataxia. nbined with other drugs having hypnotic or CNS-depressant s, consider potential additive effects. Employ usual precautions tients who are severely depressed, or with latent depression or dal tendencies. Periodic blood counts and liver and kidney ion tests are advised during repeated therapy. Observe usual utions in presence of impaired renal or hepatic function.

rse Reactions: Dizziness, drowsiness, lightheadedness, ering, ataxia and falling have occurred, particularly in elderly bilitated patients. Severe sedation, lethargy, disorientation and , probably indicative of drug intolerance or overdosage, have reported. Also reported were headache, heartburn, upset ach, nausea, vomiting, diarrhea, constipation, GI pain, nervous- talkativeness, apprehension, irritability, weakness, palpitations, pains, body and joint pains and GU complaints. There have been rare occurrences of sweating, flushes, difficulty in focusing, ed vision, burning eyes, faintness, hypotension, shortness of h, pruritus, skin rash, dry mouth, bitter taste, excessive saliva- anorexia, euphoria, depression, slurred speech, confusion, ssness, hallucinations, and elevated SGOT, SGPT, total and bilirubins and alkaline phosphatase. Paradoxical reactions, excitement, stimulation and hyperactivity, have also been ted in rare instances.

ge: Individualize for maximum beneficial effect. *Adults:* 30 mg dosage; 15 mg may suffice in some patients. *Elderly or debil- l patients:* 15 mg initially until response is determined.

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ost JD Jr: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ
gel GW: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ
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Opinion & Dialogue

Is there a need for a drug compendium?

Government Health Official

Henry E. Simmons, M.D.
Deputy Assistant
Secretary for Health
Department of Health,
Education and Welfare

A drug comp diu
of the type I en ion
would fill a defir
need for the ct
ing physician ch
compendiun o
give him t
informatio ne
essary fo s
a drug intelligently, and it w ld
do so in a clear, concise, con
venient, objective and balan d
fashion.

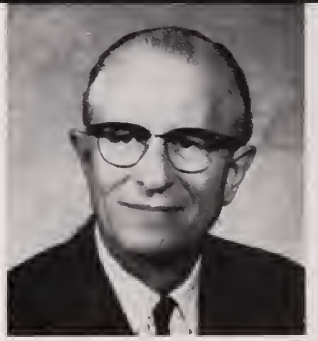
What a Compendium Should Contain

I believe the compend n
should inform the doctor wh a
drug will do, when he should s
for what type of patient, for w
long, in what dose, what ben its
his patient is likely to obtain e
risks involved, and cross-rea ion
with other drugs.

The information would e
based on the package insert d
have the same legal status. fa
a complete compendium wi co
plete and current informatio
might even eliminate the ne ss

Maker of Medicine

Joseph F. Sadusk, Jr., M.D.
Warner-Lambert Company



A drug compendium,
preferably compendia, shou l
believe, be private, not fede
sponsorship. They should co a
comprehensive listings of dr gs
available for prescribing. Th
should be single, legibly prin d
volumes of reasonable size,
dated quarterly or semiannu y
and completely revised ever e

Function of a Compendium

A compendium should r-
nish the following informatio or
drugs in the following order: di
tions for use, side effects, ac r
drug reactions, contraindica on
drug interactions, drug dosa a
the dosage forms marketed. ru
prices should not be include be
cause they vary so widely an
change rapidly.

No compendium shoul se
forth drugs of choice or disc s
relative efficacy. Such ques ns
must be left for the practicin p
sician to decide, whether on e
basis of the medical literatu h
own clinical experience, adv e
colleagues, information sup ec
by manufacturers, and so or

Nor should a compend m
undertake to educate the do or
how to use drugs. Rather, it s
be a reference source desig d
marily to refresh his memor s
drugs he may not use regula .

package insert in many in-
es. This would constitute a
antial saving for the manu-
rer.

By a complete compendium,
ot mean a volume of prohibi-
ize. You don't need a book
ribing 25,000 products with
ormous amount of repetition.
er, drugs should be arranged
ass. Mutually applicable infor-
on would be provided, along
rief discussions pinpointing
ences in specific drugs of
lass. Listings would be cross-
ed in a useful way.

Available Documents as
es of Information

Existing references such as
and the AMA Drug Evaluation
bviously useful but they are
nplete. Either they are not
-referenced by generic name
lo not group drugs with simi-
aracteristics, or they do not
l the available and legally
eted drugs. And some of
omitted may be very useful.

On the other hand, drugs made by more than one supplier, tetracycline for example, may be fully described a dozen times in the same book.

While perhaps PDR could be rearranged and cross-indexed with generics included, and while the AMA Drug Evaluation might also be modified and expanded, I am not sure that the end result would have all the attributes required for a useful compendium. At the same time, you would run the risk of amassing a voluminous and unwieldy tome.

Should Editorial Comments Accompany the Listings?

Subjective judgments, in my opinion, have no place in a compendium. However, if there is substantial evidence based on a sound body of science concerning relative efficacy of several drugs, certainly that information should be included. The committee of experts compiling and editing a particular section would also have to assess and indicate instances where a meaningful difference between drugs is pertinent.

Sponsorship, Compilation and Editing

Producing a book like this would undoubtedly be difficult and demanding. It would obviously take a great deal of talent and expertise, and would require a varied and experienced group, ranging from writers and editors to highly skilled clinicians and pharmacologists. Style, format and clarity of language would play an important part in determining the usefulness of the book. And it should be updated periodically and completely revised annually.

I have no opinion whether the government or the private sector should sponsor and/or finance the compendium. What is most important is that the compendium be an authoritative, objective and useful source of information for the doctor to have at hand as a ready reference.

---

ld in no way imply control over
ractitioner's prerogatives.

Another Compendium?

A practicable, single-volume
pendium cannot, nor is it
ssary to, include all drugs on
narket today. From my prac-
of internal medicine for some
ears, my experience as a con-
nt, and as a faculty member
ur or five medical schools, I
d estimate that a doctor uses
30 to 35 drugs regularly. The
Physicians' Desk Reference,
entally, contained about
0 entries.

As to whether there should be
eral compendium, in my opin-
as stated earlier, the answer is
—there should *not* be one. The
osal assumes that existing
pendia are inadequate. We're
ure of that at all. Whatever its
rfections, the present drug
mation system in the U.S. is
, multifaceted, pluralistic and
nsive. Good compendia exist,
ll as other ample sources on
therapy, ranging from journal
ture through AMA Drug Evalu-
to company materials. Not
ysicians may use such
ces as often or as well as they
ld, but that is the fault of the
, not of the sources.

In any event, rather than produce another book, it makes much more sense to work on improving existing compendia, and perhaps they could, as knowledge advances, include more accumulated clinical data and experience, and more information on drug interactions and adverse reactions.

Implications of a Federal Compendium

Take a hard look at the implications of a federal compendium. It would have the force of law, virtually dictating what drugs to use and how to use them. In effect, it would be a regulatory document with legal or quasi-legal status, posing medical/legal problems similar to those the doctor may now encounter if and when he departs from the provisions of the package insert. A compendium under federal aegis would tend to restrict decisions on drug therapy to one orthodox level—a most dangerous trend for medicine.

New Compendium—A Medical Option

I detect no ground swell of initiative or support whatsoever for a federal compendium—or, for that matter, for a new compendium of any type. A 1969 PMA survey conducted by Opinion Research Corporation found that only 15 per cent of those physicians interviewed felt a new compendium was needed. And a large majority did not favor the involvement of the federal government if one were to be created, preferring instead a nongovernmental consortium.

Even if we come to a time when the medical profession itself opts for a new kind of compendium, it should be handled and financed, ideally, outside both government and industry. Final review and editorial authority could be delegated, say, to specialty bodies and medical societies—but above all, *not* the government.

Surely the health care system in the United States has far more vital matters to consider than the extensive cost and effort that would have to go into the preparation and maintenance of a new, monolithic compendium, and especially one bearing the imprimatur of the federal government.

Opinion & Dialogue

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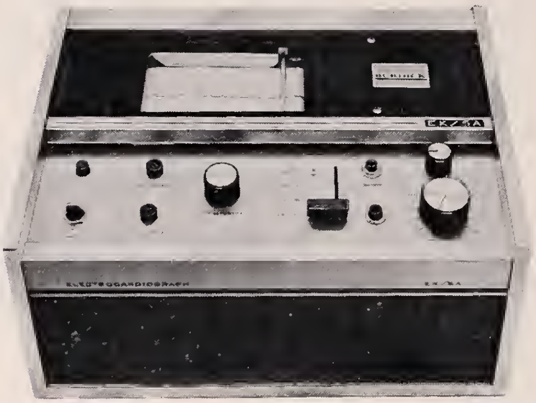

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Editorials

The Fifty Year Club

INETEEN-TWENTY-FOUR was a gay year; THE ır, a distant six years behind, and the difficul- s of the future, depression, more wars, smog, bestos in the air and in the water, Watergate, d fuel shortage, not yet on the horizon. Calvin olidge was the President, unencumbered with y Vice President.

On the local medical scene Frank Hirschboeck Duluth and Thomas Peppard of Minneapolis re writing abstracts in medicine and Leo Rigler d A. U. Desjardines' abstracts in roentgenology r MINNESOTA MEDICINE. Archibald MacLaren s President of the Minnesota State Medical sociation (MSMA); a going concern whose net rth increased from $14,320 in October, 1923, $14,845 in October, 1924. Membership num- red 1852 and they published a journal, MIN- SOTA MEDICINE, with a subsidy from each mber of $2.00.

Twenty-two members of the MSMA semicen- arians in medicine this year were inducted o the Fifty Year Club at the Annual Meeting Duluth in May. They finished their medical ining about 1924. This distinguished group ludes: Raymond N. Bieter, retired professor of armacology and perennial secretary of the sic Sciences Board; Royal Gray, who had a nd in the teaching of neurology to a dozen nerations of medical students; Arthur A. Zier- l, the eminent surgeon and head of surgery at nneapolis General Hospital for many years; rl W. Anderson, track star and insurance man o hurdled all obstacles to become a leader in profession; and many others whose distinguished records are listed elsewhere in this journal.*

Ladies and Gentlemen of the Class of 1924, all 22 of you have been and are outstanding citizens of the State of Minnesota. Your colleagues now honor you, inducting you into the most exclusive Fifty Year Club.

The following are excerpts from MINNESOTA MEDICINE, Volume 7, and the JOURNAL LANCET, Volume 44, both of the year 1924:

. . . *Hypoglycemia* by J. B. Collip, M.A., Ph.D: "The observation that a condition of hypoglycemia can be produced in a normal animal (rabbit) by the subcutaneous administration of an extract of pancreas containing the active principle was first made by the writer (Collip) in December, 1921, shortly after he became a co-worker of Banting, Best and MacLeod."

. . . *Editorial, The Proposed New Minneapolis General Hospital:*

"The present Minneapolis General Hospital in the congested downtown district of Minneapolis is too small for the growing city. But where should such a hospital be placed? Its primary function is the care of the poor of the city. For this purpose it should have good physical surroundings; but above all it should have the best staff and nursing service that can be provided. Doubtless, like all the great charity hospitals, it will be dependent on a voluntary staff. It should be placed where it can be reached easily by the busy men of the medical profession. This shuts out distant suburban proposals. The river bank near the Medical School is beautiful and accessible."

See page 483.

. . . Propaganda for Reform: *The Menace of "Moonshine" Whisky*. "The untoward results of overindulgence in whisky have usually been ascribed to its alcoholic content, although now and then ill-defined 'by-products' of fermentation present in the distillate have been charged with a toxicity out of all proportion to the quantities ordinarily present."

. . . *Problems Encountered in the Treatment* of *Disease of the Biliary Tract* by E. Starr Judd: "It has been suggested that the common duct is more prone to be the seat of stone formation after removal of the gallbladder. This hypothesis was based on the assumption that the common duct would take up the function of concentrating the bile which the gallbladder had performed, but apparently this does not occur. Recently we sent follow-up letters to one hundred patients whose gallbladders had been removed more than twenty years before, and in a study of this series we have found only one instance in which there was reason to believe that stone had formed in the common duct after the cholecystectomy. It would be entirely possible to overlook stones at the primary operation and it seems probable that these stones were in the ducts at the time of the cholecystectomy."

Dr. Strachauer: "I have never had nor seen one case of acute cholecystitis die without operation. The mortality chapter—the dark chapter—in surgery of the gallbladder has to do with acute cholecystitis. The situation is not comparable to acute appendicitis. The acutely inflamed appendix and the gangrenous appendix are prone to undergo rupture and perforation, and, of course, the diagnosis of acute appendicitis carries with it the indication for a prompt operation. Not so the acutely inflamed gallbladder. In my entire University Hospital experience and private practice I have seen only two cases of rupture of the gallbladder. We all know that operation on the acutely inflamed gallbladder is an extremely dangerous one. When the acute phase of the infection has subsided and the patient is taking fluids generously, eating and sleeping well, I go in and remove the gallbladder. The extra hazard has passed, and the patient can be safely operated upon."

. . . *Some Notes on the Treatment of Tuberculosis* by A. T. Laird: "Rest is our most powerful resource in fighting active tuberculosis. Open has no direct action on the tubercle bacillus a is only one of the many measures for increasi bodily resistance to the invading germs. Yet is one of the very best. There are very few da in the year in temperate climates when outdo life cannot be enjoyed. Automobilists find possible to be comfortable out of doors, even open cars, with the help of fur coats, foot warr ers, etc. and patients should have all necessa equipment for outdoor living. Usually, especial for those who have lived indoors, there resul a general improvement in nutrition, appetit digestion and sleep."

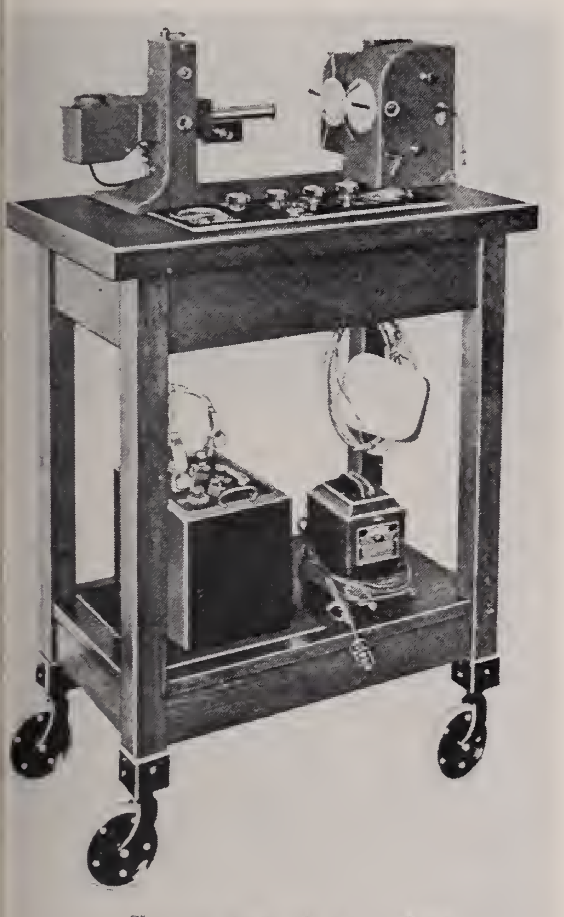
. . . *Of General Interest:* "In a recent address, D Banting related how the observation by Dr. Mos Barron of Minneapolis of the effect of exper mental ligation of the pancreatic duct led to t deduction that by this means it might be possib to eliminate the products of the acinous cells a obtain the product of the islets. Thus is researc founded upon research."

. . . *Spinal Analgesia* by George F. Thompson Chicago, Illinois: "I operated on this patie under spinal analgesia day before yesterday 9 o'clock, and you see she is in good conditio (To the patient): Did we hurt you during t operation? Answer: Yes. Question: What hu you? Answer: Somebody mashed me on the che One thing you have to be careful about is th the interne does not lie on the patient's che while helping you to operate. Internes like go to sleep leaning on the chest while you a doing a laparotomy. Right above the field operation is a zone of hyperesthesia which hur a great deal, and that is why she imagined s was being 'mashed.' "

. . . "Physician and Surgeon Wanted: In goo town and large territory. The right man can from six to ten thousand a year. For particula address E. V. Peterson, Gary, S.D."

. . . "Physician Wanted: In a town of 800 popul tion in southeastern part of North Dakota. A b territory and a prosperous country. Mostly Germans with a few Hollanders around. Doct must be able to speak German. Give referenc in first letter. A very good opening for the rig ind of a man. Address Nick Renner, Jr., Stras-urg, N.D."

. . C.P.C. Dr. Carl von Neupert, Jr., (Stevens oint, Wisconsin): "I wish to report an extremely 1teresting case. A woman, aged 63, whom I ttended for inflammation of the gallbladder last larch. She was sick three weeks, got over the ttack nicely, and was practically without symp-oms until a week ago last Saturday. She had artaken of a rich meal, commenced to vomit, nd the following day rigidity and pain over the bdomen developed. There was no rigidity or pain ı the region of the gallbladder, but there was onsiderable pain over the region of the appendix. advised her to go to the hospital that I might watch the case. She refused to do anything and begged me to give her a hypodermic of morphine, which I did contrary to my rule in abdominal cases. The following day she had vomited greenish material and continued to vomit for several days. I finally induced her to go to the hospital for high enemas. At the beginning of the second day I thought she had intestinal obstruction. Due to the washing out of the stomach and to the fact that all food and even water was withheld the vomiting let up, and she was apparently easy until late Tuesday evening when she commenced to vomit fecal material. Operation was refused until Wednesday morning when the relatives realized nothing else could be done. I operated and found . . ." (The answer will be found on page 479 . . . every medical student should know the diagnosis since all of the critical data are given by Dr. Neupert:)



The Sanborn electrocardiograph.

Figure—Modern self-contained, portable galvanometer ith built-in, rotating signal and moving photographic lm. Latest model-1924.*

. . . *Indications for the Use of Insulin* by E. L. Tuohy: "No method of the oral administration of insulin has so far been accepted, yet drug houses send their salesmen back and forth across the entire country lustily discussing how their particular company, by superior judgment and skill, is able to extract the pancreatic hormone and combine it variously, stressing their arguments for its supposed benefit by the flimsiest of clinical reports. Why, gentlemen, do we tolerate this sort of thing at the very time when we have before us the dignified attitude of Banting and Best and their co-workers."

. . . The Instrumental Recognition of Cardiac Irregularities by Harold E. Richardson: "Gradually a few instruments (Electrocardiographs) came into use in this country, and in 1912 Dr. Charles Lyman Greene, then head of the Department of Medicine at the University of Minnesota, secured the installation there of the first electrocardiograph in the Northwest. At present there are five in the Twin Cities available to all members of our profession. The high initial cost (about four thousand dollars) together with the heavy expense of upkeep and operation, limits the number of purchasers of this instrument to the individuals or groups who have a sufficient demand for it."

Reuben Berman, M.D.
Editor

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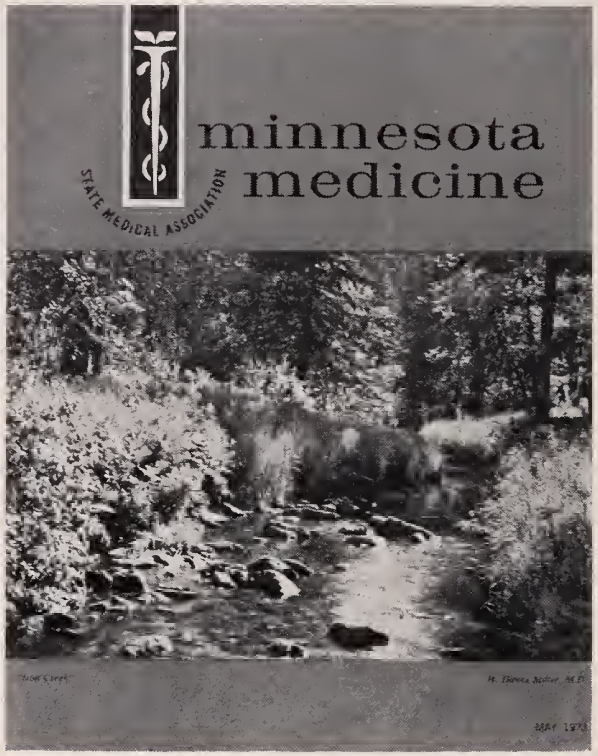
*Illustration supplied by Medtronics, Minneapolis. From: /iggers, S. J.: Principles and Practices of Electrocardiography, 90.

Pictures are Worth a Thousand Words, Three Prizes, and One Tale

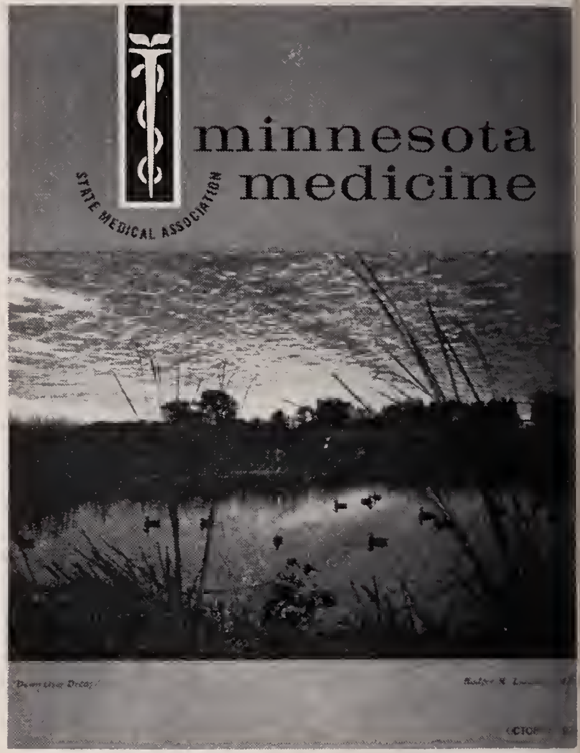
Each Spring the Board of Editors announces its choices for the best article and best cover for the previous year.

The winners for 1973 are:

Best Covers: "Iron Creek" and "Dawn over Decoys"

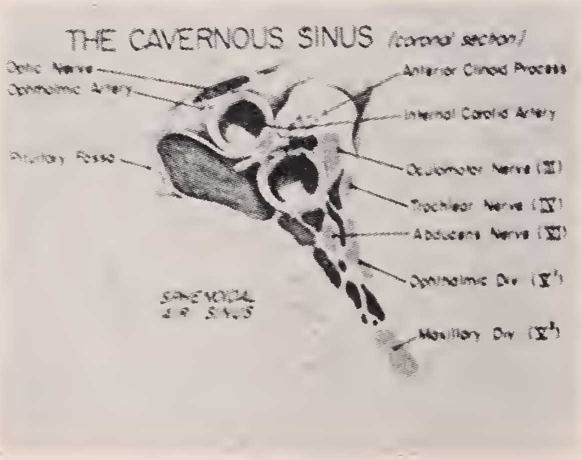

minnesota
medicine
STATE MEDICAL ASSOCIATION
"Iron Creek"
H. Dawes Miller, M.D.
MAY 1973

"Iron Creek," May 1973 issue of Minnesota Medicine, by *H. Dawes Miller, M.D.*, Director of Medical Education, Fairview Hospitals, Minneapolis.

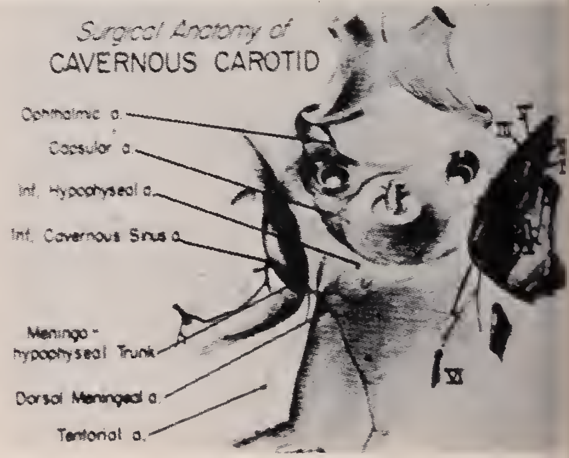

minnesota
medicine
STATE MEDICAL ASSOCIATION
"Dawn over Decoys"

"Dawn over Decoys," October 1973 issue of Minnesota Medicine, by *Rodger R. Lundblad, M.D.*, Urologist Minneapolis.

Best Article: "Carotid-Cavernous Fistula"


THE CAVERNOUS SINUS (coronal section)
Optic Nerve
Ophthalmic Artery
Pituitary Fossa
Anterior Clinoid Process
Internal Carotid Artery
Oculomotor Nerve (III)
Trochlear Nerve (IV)
Abducens Nerve (VI)
Ophthalmic Div (V¹)
Maxillary Div (V²)
SPHENOIDAL AIR SINUS

Cavernous Sinus


Surgical Anatomy of
CAVERNOUS CAROTID
Ophthalmic a.
Capsular a.
Inf. Hypophyseal a.
Inf. Cavernous Sinus a.
Meningo-hypophyseal Trunk
Dorsal Meningeal a.
Tentorial a.
VI

Cavernous Carotid

Anatomical Line-Drawings from "Carotid-Cavernous Fistula," by *Edward L. Seljeskog, M.D.*, Associate Professor of Neurosurgery, University of Minnesota, in Minnesota Medicine, November, 56:929, 1973.

One Tale

Why three prizes instead of two—one for best article and one for best cover? Why two covers nstead of one? After all, the Board usually choses one cover.

There hangs a tale about Doctor Reuben Berman, Editor of MINNESOTA MEDICINE. Doctor Berman takes a quiet pride in the quality of the overs and in the work of Doctor Farrell S. Stiegler, a member of the Board of Editors, who ssiduously collects, sorts, and selects the proper over for a given issue. Doctor Berman likes to praise good work. So, while the Board was selectng its cover, Doctor Berman was praising the overs to Samuel Sachs, Director of the Mineapolis Institute of Arts. Doctor Berman even sked Mr. Sachs to pick the best cover.

As individual choice and varying taste would ave it, the Board and Mr. Sachs picked different overs. This led to a political problem for Doctor Berman: Should he take the choice of the Board, whose taste he respects, or should he go with the hoice of Mr. Sachs, whose taste no one quibbles with?

Being a resourceful politician, peerless in maters of peer diplomacy, Doctor Berman simply old the Board there were two winners. But he idn't tell the Board which one they chose and which one Mr. Sachs chose. Nor am I going to tell you which is which because Doctor Berman hasn't stated which was which. This, as Doctor Berman has plainly indicated, isn't a which hunt. There hangs the tale. Let it lie.

Best Articles

I have no tale to tell about the best article. Doctor Seljeskog simply wrote an excellent paper. He opened by mentioning the striking signs of symptoms of carotid-cavernous fistula; offered a couple of historical vignettes; illustrated the anatomy, signs, and symptoms; ran down the differential diagnosis, and closed by going step by step through varying ways to manage the problem.

What stands out, however, is the quality and relevance of illustrations in Dr. Seljeskog's article. The article contains those excellent anatomical line drawings of carotid-cavernous fistulae, ten closeup photographs of the striking chemosis, several scleral injection, orbital edema and exophthalmus evoked by the fistula and eight carotid angiograms of representative cases.

All in all, a superb example of a well-constructed, beautifully illustrated medical article.

We congratulate Doctor Seljeskog and the cover winners, Doctors H. Dawes Miller and Rodger R. Lundblad.

Richard L. Reece, M.D.
Minneapolis, Minnesota

Intrauterine Device

Contraceptive or Abortifacient

HILGERS* HAS WRITTEN a superb, comprehensive nd well organized review of our current knowldge concerning the mode of action of the intraterine device. Though the ideas expressed are ot new ones, this is the most complete summary hat I have seen which concerns itself primarily with the mode of action of the IUD. It is quite lear that the effectiveness of the IUD is attributble to the sum of its effects on contractility paterns, electrical potential, and histologic, cytologic nd biochemical changes in the endometrium and ntrauterine melieu. There is little doubt that Mastroianni's[†] original suggestion that the acion of the IUD was on tubal motility and ovum transport is now passe. Most authors agree with Hilgerts' contention that the device, by its action on the many parameters discussed, in some way interferes with the development or nidation of the blastocyst. If this concept is not acceptable to a patient or her physician on moral or religious grounds, another method of fertility control should be chosen.

The ideal contraceptive that is 100% effective, simple to employ, totally safe, inexpensive, reversible, acceptable to all who would desire to use it, and does not require preparation for each act of coition, has yet to appear on the horizon. The IUD is only one of several methods which approach but still fall short of this ideal by varying degrees. While awaiting its arrival (the ideal contraceptive), physicians must be cautioned against jumping on the band wagon of every new pill, device, or gadget that comes on the scene.

Thomas C. Carrier, M.D.
Minneapolis, Minnesota

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[*] See page 493.

[†] Mastroianni, L. Jr. et al: Mechanism of action of the intraterine contraceptive device in the primate. Intra-uterine Contraeption. Proceedings of the Second International Conference 1904. xcerpta Medica Foundation.

Fractures of the Sacrum*

FRACTURES OF THE SACRUM are so rare that textbooks may only mention them. If a marked displacement of the sacrum should occur following the fracture the only nerves involved would be those that make up the sacral plexus; that is, the nerves that make up the plexus below the fracture.

Conservative treatment is indicated for fractures of the sacrum. Substantial hemorrhage may be encountered, but this can be counteracted by the use of the appropriate blood replacement. As a rule, the only treatment indicated is supportive until the fracture has gone on to healing and the patient ha been relieved of his subjective complaints.

Certainly a marked displacement of a fractur of the sacrum might require some type of manipulative reduction. In my experience I have neve encountered this, and after a review of the literature I find that it has not been necessary.

Fractures of the sacrum are rare and conservative treatment should take care of the great majority of these fractures. Fractures of the sacrun should go on to healing without any disability.

Harry B. Hall, M.D
Minneapolis, Minnesot

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*See page 465.

The Naked Eye and Other Bare Necessities

THE APRIL ISSUE OF MINNESOTA MEDICINE* contains a piece, "The Use of Microscopic Filters in the Administration of Intravenous Fluids," that caught my eye.

Why? For the simple reason the authors, two keen-eyed laboratory technicians and an Associate Professor with vision, used their retinas to record basic observations. What they saw wasn't much: foreign particles in intravenous fluids. But they put what they observed to good use. They inserted filters to rid particles from the fluid.

Furthermore, the authors unabashedly say: "To assess the practicality of using such filters, the last thirteen filters used as well as two unused filters were inspected with the unaided eye as well as with magnification of either 30X o 100X".

So it's come to that: medical observers usin the naked eye to make observations. Next thin you know we'll be using our ears to listen, ou noses to smell and our fingers to feel—lowerin ourselves to the bare necessities.

Next time something streaks before your eyes. write about it and send your piece to us. We just might publish it.

Richard L. Reece, M.D
Minneapolis, Minnesot

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*Page 325.

New Editor-in-Chief of MINNESOTA MEDICINE

Dr. Reuben Berman will retire as Editor-in-Chief of MINNESOTA MEDICINE at the end of this year, and the Council is interested in hearing from any physicians who would like to be considered for this position. It is hoped that a new editor can be chosen by September 1. Address communications to: Council, 375 Jackson, St. Paul 55101.

R. J. Frey, M.D.
Chairman, Council

It's A Pleasure to Serve You

"For the son of man also came not to be ministered unto but to minister . . ." Mark 10:45.

S O RUNS THE verse embossed on a plague or arved in stone in many of our modern hospitals. And often, within a few steps, stands a handsome mahogany-and-glass machine, so infallibly automated that it will instantly dispense not only our brand choice but also exact change for any overpayment into its slots. A paragon of technological achievement—albeit a minor one!

"As a service to their patients" these machines net only an insignificant monetary profit to the ospitals whose lobbies or halls conspicuously eature them. Since such an automation disgorges in excess of 150,000 cigarettes annually—and assuming that it requires an average of one pack a day for 20 years (146,000 "coffin nails") for an individual to develop lung carcinoma—does it not follow that each one of those tax-free "health nstitutions" might well be guilty of contributing o the development of more than one lung cancer annually, "As a service to their patients?"

Paradoxical? Not without sound reason has Michael Kammen called us Americans "people of paradox" who *profess* but do not *practice.*

But someone will be sure to ask: How about he morale of the patient who smokes? Is that not as important to his recovery as adequate proessional care by doctors and nurses? But to couner that: How about the morale of the nonmoker exposed to fumes he detests? Ironically, he smoker's morale has, on occasion, taken precedence over the abstainer's, for non-smokers have been known to be told to change rooms when they have voiced objection to the foul and unhealthy emanations from one of their four-bed-patient roommates.

We must not forget that, a station or two farther down the hall, the hospital, in its benevolence, has installed a $150,000 Intensive Care Ward where the inoperable cancer-of-the-lung patient can be kept alive for a few more agonizing weeks than Nature alone would bequeath him under the circumstances.

Not entirely analogous but reminiscent, in this context, is the case of the researcher who daily applied a bit of carcinogenic tobacco tar to his hapless laboratory animals while simultaneously inhaling smoke from his own favorite brand of cigarettes. One might speculate sardonically on the ambiguity of the situation. Clearly the researcher was the *experimenter.* But was he conducting *one* or *two* experiments? And who were the *experimentees?*

With this brief philosophical musing I must, in conclusion, yield to the futility of advising and abdicate to the bravado of the "hooked" smoker when he replies to my dire prognosis: "Well, I guess that's the price I'll have to pay for the pleasure I derive." So be it! For who am I to presume to deprive an individual of a choice pleasure; to exhort a health institution to practice its own preaching; to worry or harry a spouse whose mate persists in a pernicious habit. Perhaps, after all, a man has a right to choose a protracted, agonizing demise over any other kind—if that be his pleasure.

Carl O. Rice, M.D., Ph.D.
Editor Emeritus

Answer to C.P.C.

From page 475.)

"An impacted gallstone in the small bowel, but ust exactly where it was located in the small bowel I did not take time to find out, but because of the fact that I had to deal with several feet of bowel I take it that it was three or four feet down anyway. The stone was as large as a good-sized egg."

Letters to the Editor

Dear Editor:

I appreciate Dr. Klain's editorial* comments about the article "Meconium Aspiration in the Newborn."[1] I believe there are a few points that need clarification and reemphasis:

If anticipatory management is practiced and the set-up for lavage is ready at each meconium stained delivery—the added fifteen seconds for lavage *after* adequate suctioning does not constitute an unwarranted delay. This is assuming that adequate suctioning of the trachea includes intubation.

In the study, Tracheobronchial Lavage in Small Infants,[2] the PaO_2 was lowered only in our initial case. The PaO_2 was not lowered when the technique was modified. It is this modified technique which is recommended for use in the delivery room. If performed as described, it should not increase the risk for the infant and may be helpful.

Martha Burke Strickland, M.D.
Uvalde, Texas

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*Klain DB: Meconium Aspiration in the Newborn. 56:1054, 1973.

References

1. Strickland MB: Meconium aspiration in the newborn, Minnesota Medicine 56:1031-1035, 1973.
2. Strickland MB: Tracheobronchial lavage in small infants, Minnesota Medicine 56:287, 1973.

Dear Editor:

Dr. Maslansky* is incorrect in stating that there is no required teaching of substance abuse at the University of Minnesota Medical School, Minneapolis. There are, in fact, required hours devoted to alcoholism and to drug abuse in both the first and second medical year programs, in pharmacology and in human behavior. Further, and by way of responding to concern expressed by the Minnesota State Medical Association, among others, additional required hours have been added to the second year program this spring so that a front line experience with the clinical aspects of care of patients with substance abuse will be available for each student. In addition, Dr. Joseph Westermeyer, Assistant Professor of Psychiatry and recipient of a National Institute of Health grant on Drug and Alcohol Abuse, has begun long-range planning toward the development of a comprehensive education program in this field. While Dr. Maslansky calls for attention to emergency room diagnosis of chemical abuse and to referral, a medical student-faculty group at Minnesota has requested and are receiving teaching aimed at a more comprehensive series of educational objectives: (1) help others (diagnosis, proper referrals); (2) help self (recognition of hazards to certain high stress professions, including physicians) and (3) eliminate some of the problem (contribution by the physician to over use of medications by patients).

Robert J. McCollister, M.D.
Assistant Dean
University of Minnesota
Medical School

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*Maslansky R: Emergency room experience with chemical abuse. Minnesota Med 57:108, 1974.

Dear Editor:

It was indeed a pleasure to read Dr. John Seymour's editorial comment* on my article, The Management of Pain with Nerve Blocks, which appeared in the March, 1974 issue of MINNESOTA MEDICINE. I agree in entirety with everything he said; it, in fact, was a great pleasure to read comments such as his from a person who obviously has had experience with diagnostic nerve blocks, surgical rhizotomy and chronic pain problems.

He brings out a fascinating point. That is the patient totally anesthetized below the nipple line being unable to move or to feel a severe noxious stimulus in the foot, and yet persisting in complaints of foot pain. These are indeed difficult problems. I would like to hear any further thoughts he might have concerning them.

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*Page 223.

With patients we see and evaluate at the Pain Clinic here in Seattle, I am impressed that very often these "central pain states" occur because an adequate neurological exam was not done after a high spinal block, with the result due to arachnoiditus, scarring or whatsoever, they were sparing of sensory input to the cord usually over the S2 root. Central pain itself however, except for that seen in the severe schizophrenic, or associated with the thalamic syndrome, is in my experience controlled by reducing peripheral input, hence, many manipulations from nerve blocks to destructive lesions such as rhizotomies do result in temporary relief. It is amazing the ability of the nervous system to circumvent our efforts and reestablish the prior situation, however, maybe Dr. Fordyce in his article had some solution to this.

Richard G. Black, M.D.
Coordinator, Pain Clinic
University of Washington

Dear Editor:

Dr. Black brings up a very interesting point in his letter. The nerve root that is least likely to be infiltrated by the Pontocaine when one does the graded isobaric spinal block is the nerve root that is heavily covered by scar tissue. In such a situation can you ever be absolutely certain that all pain fibers from the extremity have been blocked? Can one ever be certain that the neurological examination that he has done is complete enough?

I frankly think I have seen what I would call central pain in a number of situations. The thalamic pain syndrome of Dejerine-Roussy which Dr. Black mentioned is an obvious example and proof of the fact that physical alterations in the central nervous system can be responsible for pain; and why not other alterations? Where does the pain come from in the patient with a conversion reaction who has a painful paralyzed leg, who has a normal EMG, and a normal lumbar myelogram? This too, seems to be central pain.

As an aid in evaluating the amount of secondary gain involved in the chronic pain problems, I have found the following question very helpful during the history and physical examination: "What does this pain keep you from doing?" For example, if you were told that "This pain is so bad that it keeps me from washing the walls and scrubbing the floors which I really like to do," then whether that statement is true or not the prognosis for relieving this patient of her complaint with any amount of surgical or physical manipulation is very poor indeed.

Finally Dr. Black's position and mine in regard to pain interpretation rather represent, at least for this discussion, the poles of pain interpretation, the peripheral and the central. The obvious situation is that pain arises from a distinct lesion in the periphery and is interpreted centrally—and this has been thoroughly taught. There are, however, some pain situations in which the pain seems grossly out of proportion to the lesion presumably responsible for the pain, in which there seems to be some central component. Two aphorisms, not original with me I hasten to add, serve to illustrate this problem: The first, "Pain long enough established tends to become independent of the stimulus;" and second, "Some people seem to need their pain despite their protestations that it be removed." (I have had a patient, who, when her pain was transiently relieved by hypnosis, would later that evening have attacks of anxiety followed by a pronounced worsening of her asthma.)

John L. Seymour, M.D.
Minneapolis, Minnesota

Continuing Medical Education

In cooperation with the Minnesota State Medical Association's continuing education plan, MINNESOTA MEDICINE invites all organizations sponsoring continuing education programs for physicians in Minnesota to list the details of these programs in the journal. We will list these up to one year in advance of the program, and need the information two months prior to the monthly journal in which the details will appear.

Please send the complete form to:

Reuben Berman, M.D.
MINNESOTA MEDICINE
375 Jackson St.
St. Paul, Mn. 55101

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Fifty Years of Faithful Service

KARL W. ANDERSON, M.D.

Dr. Anderson retired about six years ago after 30 years as senior vice president and medical director with the Northwestern National Life Insurance Company. He was treasurer of the Minnesota State Medical Association for 11 years and currently serves on the Board of Editors of MINNESOTA MEDICINE and as an ex-officio member of the Committee on Hemodialysis and Transplantation. He is a past president of the Minnesota Medical Foundation, Minneapolis Academy of Medicine and the Minnesota Heart Association and has devoted much service to the United Fund and Red Cross. In addition, Dr. Anderson has served many other medical organizations and particularly enjoys helping youngsters enter the fields of medicine. He received the Harold S. Diehl Award in 1965 and the Association's Distinguished Service Award in 1966 as well as special awards from the Minnesota Heart Association and the American Red Cross. Doctor Anderson graduated from the University of Minnesota Medical School in 1924, did postgraduate study there in internal medicine and interned at Minneapolis General Hospital and Abbott Hospital. During his college years, Doctor Anderson captained the University of Minnesota track team and in 1924 became the first Minnesota member of the Olympic team. He was the national champion of both indoor and outdoor high hurdles.

MARKHAM J. ANDERSON, SR., M.D.

Dr. Markham Anderson was a delegate to the State Association from the Zumbro Valley Medical Society for seven years and its president in 1946. Born in Rochester in 1895, he was graduated from the University of Minnesota Medical School in 1925 and became a fellow at the Mayo Foundation the same year. In 1929, he was appointed to the Mayo Clinic staff as a consultant in medicine, retiring from the Mayo Clinic in 1961.

HOMER P. BASINGER, M.D.

Dr. Basinger began practice in Windom in 1924. He is in family practice, served the city as health officer and has also been the medical examiner of the national guard. Doctor Basinger was born in Columbus Grove, Ohio. He attended the University of Chicago and Northwestern University Medical School, Evanston, Illinois and interned at Wesley Memorial Hospital, Chicago.

ANTHONY J. BIANCO, SR., M.D.

Dr. Bianco practiced as a general surgeon in Duluth. He attended the University of Wisconsin and the University of Minnesota Medical School. Dr. Bianco interned at St. Mary's Hospital, Duluth, and remained in Duluth until he retired from practice. In 1956, he was president of the St. Louis County Medical Society and in 1949 was vice-president of the Interurban Academy of Medicine.

RAYMOND N. BIETER, M.D.

Dr. Bieter was secretary-treasurer of the Minnesota State Board of Medical Examiners. He is a 1923 graduate of the University of Minnesota Medical School and a graduate student in the Department of Pharmacology. In 1925 he joined the faculty becoming head of the Department of Pharmacology in 1943. Dr. Bieter in 1962 was made director of special education services in the medical school dean's office and retired in 1969 after 45 years of service to the University.

LUCIAN G. CULVER, M.D. (deceased)

Dr. Culver, ophthalmologist, and a 1925 graduate of the University of Minnesota Medical School interned at Charles T. Miller Hospital. He practiced in Stillwater, Thief River Falls and Eau Claire, Wisconsin, before entering the Navy in 1946. One and a half years was spent in the Pacific Theater as chief medical officer aboard a transport. In preparing for ophthalmology, Doctor Culver attended the University of Vienna, Austria and Howard University, Washington, D.C.

GEORGE D. EITEL, M.D.

Dr. Eitel, surgeon, still practices across the street from Eitel Hospital where he has been located for 50 years. Graduated from the University of Minnesota in 1924, he received his post-graduate training at the University of Berne, Switzerland and in Freibourg, Germany. In 1928, he returned to Minneapolis to continue his uncle's surgical practice at Eitel Hospital. He was appointed surgeon for the Minnesota State Board of Control and was affiliated with the University of Minnesota Medical School, Department of Surgery in 1933, retiring in 1967 as Assistant Professor of Surgery. Doctor Eitel is a diplomate, American Board of Surgery, and a member of the American College of Surgeons and Minneapolis Surgical Society. He likes gardening and landscaping.

EDWARD K. ENDRESS, M.D. (deceased)

Dr. Endress was born in Germany, son of a physician. He came to St. Paul at the age of 21, graduated from the University of Minnesota Medical School and interned at Ancker Hospital. Dr. Endress was in family practice in St. Paul from 1924 to 1964 and was the founder of Riverview Memorial Hospital becoming its first chief of staff. He was the vice president of the medical and surgical staff of West Side Hospital in 1938 and also served in the navy and naval reserve.

ROYAL C. GRAY, M.D.

Dr. Gray practiced in Graceville and Cook from 1925-1928 before returning to the University of Minnesota to do postgraduate work in neurology and psychiatry. He is a member of the Central Neuropsychiatric Association and American Academy of Neurology and a former secretary-treasurer for 20 years and president in 1956 of the Minnesota Society of Neurology and Psychiatry. Dr. Gray was chief, neurology service, Minneapolis Veterans Administration Hospital, 1950-1967, and is currently professor emeritus of neurology, University of Minnesota Medical School.

MILTON B. HEBEISEN, M.D.

Dr. Hebeisen practiced in Chaska for nearly all of the 50 years he has devoted to medicine. He was graduated from the University of North Dakota and the University of Illinois and did postgraduate work at Johns Hopkins University, Baltimore; at the University of Berne, Switzerland; in Vienna, Austria; and at Cook County Medical School, Chicago. Dr. Hebeisen was president of the Scott-Carver County Medical Society and served Carver County as Health Officer for nearly 35 years.

GORDON C. MacRAE, M.D.

Dr. MacRae was honored as the physician of the year by the Governor's Commission on Employment of the Physically Handicapped in 1970 and has given dedicated service to handicapped persons in the Duluth area. From 1958 to 1973 he was medical director of the Nat G. Polinsky Memorial Rehabilitation Center, Duluth, and has been active with the National Rehabilitation Association, New York's Institute for the Crippled and Disabled, University of Minnesota Continuation Center, Sister Kenny Institute, and Duluth Advisory Committee for Vocational Rehabilitation. In 1970, he terminated his practice and became director of rehabilitation services at Miller Memorial Hospital. Doctor MacRae was born in Minneapolis in 1898 and has practiced in Duluth since 1925. He is a graduate of the University of Minnesota Medical School. During World War I he enlisted and served with the medical corps and in World War II he was promoted from major to colonel and became the commanding officer of the 347th station hospital and 53rd General Hospital in England. He is a former president of the St. Louis County Medical Society.

CLIFFORD R. MYRE, M.D.

Dr. Myre practiced in Paynesville from 1925 to 1971. He served briefly in World War I with the U.S. Navy. In 1925, he was graduated from the University of Minnesota Medical School and interned at University Hospitals, Minneapolis General Hospital and Swedish Hospital. Before moving to Paynesville, he practiced in Eden Valley for a short time. Doctor Myre is in family practice and is a member of the Minnesota Academy of Family Practice.

HARVEY NELSON, M.D.

Dr. Harvey Nelson, one-time Minneapolis surgeon, was medical director for the Soo Line Railroad for many years prior to his retirement in 1966. A University of Minnesota Medical School graduate, Doctor Nelson interned at Minneapolis General Hospital, and served a preceptorship with Doctor George R. Dunn for six years. He is a member of the American College of Surgeons, Minnesota Surgical Society, Minneapolis Surgical Society, Minneapolis Academy of Medicine, Industrial Medical Association and the Association of American Railway Surgeons. He chaired the Medical Advisory Committee of the Minnesota State Medical Association and the Committee of Direction Medical Section A.A.R. 1965-66.

LILLIAN E. PARSON, M.D.

Dr. Parson has served Elbow Lake for over 50 years, 48 of them closely with her husband. Doctor Parson attended the University of North Dakota Medical School and completed her training at the Illinois Medical School, Chicago. She interned at Womens Hospital for Women and Children, Boston, in 1921, and the Illinois University Hospital, Chicago, 1922-23. While in college she belonged to Kappa Alpha Theta and in medical school to Alpha Epsilon Iota Medical Sorority. She has been an Eastern Star since 1916, and is active in her church, and is a member of the Elbow Lake Study Club.

EDWARD N. PETERSON, M.D.

Dr. Edward Peterson co-founded the Lenont Peterson Clinic in 1936. Previously, he practiced in Buhl; Tulsa, Oklahoma; and Eveleth, retiring in 1971. Dr. Peterson received his undergraduate education at the University of Wisconsin and his medical education at the University of Minnesota Medical School, interning at Ancker Hospital. He is a member of the American College of Surgeons, Minnesota Surgical Society, Industrial Medical Association and the Great Northern Railroad Medical Association and is very active in his community. Among his many activities he lists the Virginia Chamber of Commerce, president, 1944; director of Junior Achievement; and elder, First Presbyterian Church.

JACOB A. POLZAK, M.D. (deceased)

Dr. Polzak was born in Austin and attended the University of Minnesota, graduating from medical school in 1924. He did postgraduate study at Minneapolis General Hospital in gynecology, urology and surgery. Doctor Polzak served in France during the First World War and is a member of the North Central Branch of the American Urological Society and a fellow in the American College of Surgery.

LOUIS E. PRICKMAN, M.D.

Dr. Prickman devoted much of his early career to clinical studies of brucellosis and was certified as a specialist in internal medicine with a particular interest in allergy. He is considered a major contributor to the investigations of asthma and did important studies on bronchostenosis and bronchitis. In addition he is a pioneer in the development of the practice of periodic health examinations for business executives and most recently contributed to treatment measures of patients seized with anaphlactic shock. A native of Navarre, Ohio, Doctor Prickman attended the University of Pittsburgh where he received his medical degree. He served in World War I and interned at Mercy Hospital, Pittsburgh. He came to the Mayo Foundation in 1924 as a fellow in medicine, concentrating his graduate work on general medical and surgical diagnosis, neurology and pathologic anatomy. Through a series of advancements, Doctor Prickman became head of a section of medicine and, in 1959, senior consultant in medicine. At the University of Minnesota Medical School, Doctor Prickman advanced to associate professor in 1948. He is a fellow of the American College of Physicians and a member of the Central Clinical Research Club, the Central Society for Clinical Research, the Minnesota Society of Internal Medicine, the Southern Minnesota Medical Associaton, Alpha Omega Alpha, Phi Rho Sigma and the Alumni Association of the Mayo Foundation.

WILLIAM B. RICHARDS, M.D.

Dr. Richards retired from practice in 1973. A pediatrician, Doctor Richards is a graduate of Carleton College, Northfield, and the University of Minnesota Medical School. He served his residency at Children's Mercy Hospital, Kansas City, Missouri. In 1918, he left college to join the navy and at the end of the war continued his medical education. He is a diplomate of the American Board of Pediatrics and a member of the Northwest Pediatrics Society.

HENRY A. ROUST, M.D.

Dr. Roust, a former president of the Camp Release District Medical Society, served as a delegate to the Minnesota State Medical Association and on several of its committees. He was health officer for Montevideo and is currently health officer of Chippewa County. From 1953 to 1956 he was Montevideo's mayor. Dr. Roust graduated from the University of Minnesota Medical School and interned at Ancker Hospital. During World War I he served with the army for two years and from 1925 to 1926 was with the U.S. Army Medical Corps. He commenced practice in Montevideo in 1928 and actively practices today. Doctor Roust is an expert ornithologist and enjoys treks about the woods in winter.

HOBERT J. SETZER, M.D.

Dr. Setzer, now retired, was a family physician in St. Paul. He was president of the Ramsey County Academy of Family Practice. A 1924 graduate of the University of Minnesota Medical School, he interned at St. Mary's Hospital, Duluth. Dr. Setzer moved to St. Paul and established a practice in 1926. From 1963 to 1967, he served on the Governor's anti-pollution council and in 1963 founded a nature center for outdoor teaching.

HAROLD E. WILMOT, M.D.

Dr. Wilmot was a former secretary and president of the Kandiyohi-Swift-Meeker County Medical Society. A senior member and organizer of the Litchfield Clinic, he began practice in Litchfield in 1924. He is a graduate of the University of Minnesota Medical School and is a family physician and served in the army during World War I. Doctor Wilmot is a member of the Kiwanis Club, a past president of the Litchfield Chamber of Commerce and a member of the Planning Commission of Litchfield. He is active in many civic affairs and recently, the Lion's Club honored him with its Distinguished Citizen Service Award.

ARTHUR A. ZIEROLD, M.D.

Dr. Zierold has been closely and actively associated with education throughout his career. When only 15 years old, he entered the University of Minnesota Dental School but upon graduation was too young to secure a license so he served as an apprentice. Later he began a private practice of dentistry in Minneapolis and taught in the University of Minnesota Dental School. His interest and work in surgical repair of cleft palates and congenital lip deformities led him back to medical school, and from 1919 to 1922 he held a University fellowship in surgery. His thesis concerned the electrolytic action of metals in tissue, a basic step in the development of metallic prosthetic devices so widely used today. In 1928, Doctor Zierold studied in Europe. Returning to Minneapolis, he became chief of the surgical service at Minneapolis General Hospital. In 1946 Dr. Zierold collaborated with Drs. N. K. Jenseen, Luverne Johnsrud and M. C. Nelson in the development of the treatment of compound fractures with the use of sulfanilamide and received national acclaim. A member of many local, national and international surgical societies, he is also a founding member of the Minneapolis Surgical Society and the American Board of Surgery. Currently, he is a professor of surgery at the University of Minnesota. In 1963, Doctor Zierold was presented the St. Barnabas Bowl when 18 states noted his medical contribution and leadership.

X-ray Conference

An Eleven-Year-Old Boy with Right Hip Pain

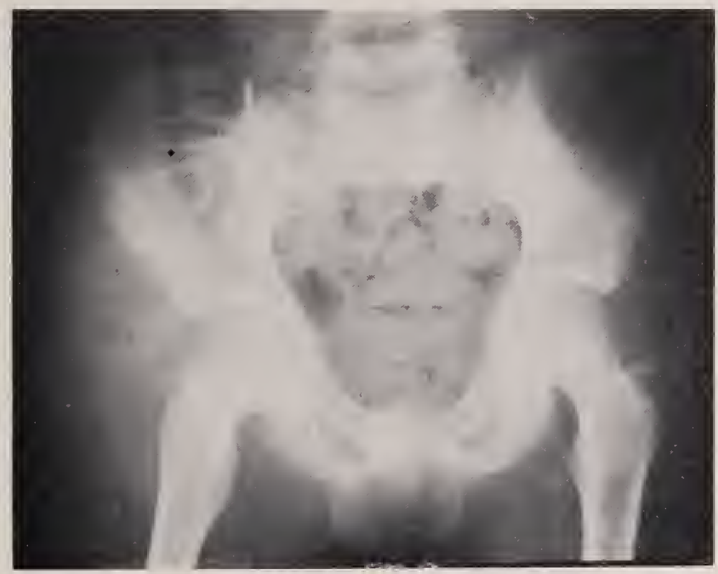
An 11-year-old boy was admitted to the hospital on October 9, 1973, with a one-day history of pain in the right hip. There was no history of trauma.

The patient had a definite limp. There was tenderness and guarding just above the right greater trochanter. The white blood cell count was 16,400 with 85% polys. The sed. rate was 20 mm./hr. Radiographs of the pelvis and hips were negative on admission.

In the hospital, symptoms continued; slight fever occurred in the afternoons. After several days, the sed. rate was 74 mm. Two right hip aspirations were cultured with negative results. Repeat radiographs on October 15, 1973 were negative.

The radiograph of the pelvis shown below (Figure 1) was another repeat examination made after 14 days in the hospital with persisting right hip symptoms. Two days after this x-ray examination, exploratory surgery and biopsy was carried out.

What is your diagnosis? (See next page.)



Figure

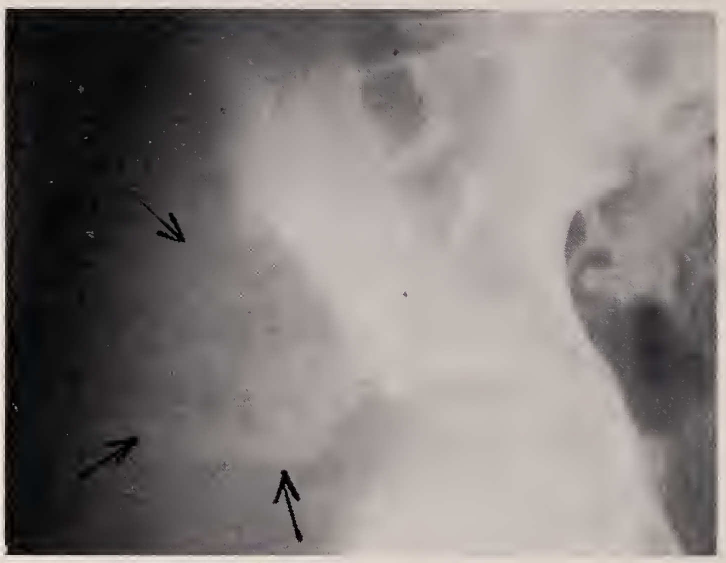


Fig. 2—The faint soft tissue calcification above the right hip is better shown in this figure which is augmented photographically.

Diagnosis: Myositis ossificans, right gluteal region.

Discussion and Diagnosis

At surgery, a bony hard mass was found just under the right gluteus medius muscle. Although grossly there seemed to be invasion of muscle, the tumor mass shelled out readily by blunt dissection. The tumor did not appear to be invading bone.

A frozen section interpretation was that the tissue was highly malignant tumor. However, after viewing the permanent sections, the tissue diagnosis was changed to benign myositis ossificans.[1,2]

Five months after surgery, the patient is doing well, symptoms have subsided and residual calcification in the region of the lesion is clearing.

The clinical story of spontaneous pain and signs of inflammation without trauma is likely to confuse the diagnosis in this type of case. Some authors have suggested that this type of lesion may be due to infection and have proposed calling it "pseudomalignant osseous tumor of soft tissue."[3]

It is important that the pathologist be aware of this possibility since, at certain stages, the abundant proliferating cells resemble malignancy. A coordinated approach between clinician, radiologist and pathologist will aid in management.

William A. Wilcox, M.D.
Department of Radiology
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Minneapolis, Minnesota

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Legal Medicine

Release of Confidential Patient Information to Carriers and Other Third Parties

JULE M. HANNAFORD, Attorney

COMMUNICATIONS BETWEEN a physician and his patient and other medical information received by a physician in the course of examination and treatment of a patient are confidential, and the physician may not ethically disclose such information to third parties without the consent of the patient, unless she is required to do so by law or unless it is necessary to do so in order to protect the welfare of the patient or the community. The State Board of Medical Examiners is authorized to revoke, suspend or restrict the license of a physician who willfully betrays a professional secret and might well take such action against a physician who fails or refuses to abide by the principle of confidentiality. Nevertheless, physicians are being faced with an increasing number of requests for patient information from insurance companies and other interested third parties, many of which seem to threaten this broad principle of confidentiality.

It should be noted that the following discussion relates only to physicians who examine and treat a patient at the patient's request. It does not apply, for example, to physicians who examine a patient at the request of an insurance company or of a defense attorney. Nor does it apply in workmen's compensation cases to employers' physicians who examine an injured employee or neutral physicians employed by the Commission to examine an injured employee.

The request of a treating physician may come from an insurance company, Blue Shield, Medicare or a local Welfare Board. No matter from whom the request may come, a physician should respond by stating that he cannot answer the request until he has been furnished with an authorization for release signed by the patient or, if the patient is incompetent or dead, signed by the patient's guardian or executor. It is the responsibility of the person seeking the information, and not that of the physician, to obtain the appropriate authorization for release of information.

Some insurance companies have on occasion requested on the telephone medical information with respect to a patient before the physician has been furnished with an appropriate authorization for release. Such a request should be treated like any other request and, even if the physician has an appropriate authorization in his files, he should avoid any disclosure over the telephone unless he is certain of the identity of the caller and of the fact that the authorization permits disclosure to the caller. Unfortunately it appears that the insurance industry has no guide to govern the conduct of insurance investigators in such situations.

Some insurance companies have taken the position that patient authorization is not necessary in Workmen's Compensation claim situations, apparently relying on a 1965 Minnesota Supreme Court decision to the effect that the physician-patient privilege does not apply in Workmen's Compensation proceedings. The physician-patient privilege is a creation of statute, however, and relates only to the relatively narrow question of whether the physician may be allowed or compelled to testify in court over his patient's objection. The fact that a physician might be called and compelled to testify in a formal legal proceeding before the Workmen's Compensation Commission does not alter the confidential nature of patient information nor does it authorize the physician to release such information voluntarily to the carrier in advance of institution of proceedings before the Commission.

With respect to request for information about Medicare patients, it should be noted that Form SSA-1490, Request for Medicare Payment, contains an authorization for release of information to the Social Security Administration and its intermediaries or carriers. The patient must sign this form before payment can be made. If the physician has taken an assignment of the patient's right to collect from Medicare, he will have in his files a copy of Form SSA-1490 signed by the patient and on the basis of the authorization contained therein is authorized to release all information needed for the claim set forth on this particular form or "a related Medicare claim." If the physician has not taken an assignment, he may or may not have in his files a copy of Form SSA-1490 signed by the Patient. If he does not have such form in his files, he should ask that a photo copy be furnished to him. Once he receives such a copy, he may release the requested information because Form SSA-1490 states that the patient authorizes a copy of the authorization to be used in place of the original.

With respect to requests from a County Welfare Board for information about a Medicaid patient, the situation is a little more complex. The law gives the Commissioner of Welfare the power to require "such reports, information and audits of medical vendors as he deems necessary." Therefore the Commissioner could issue a regulation requiring physicians to hand over to County Welfare Boards such confidential medical information about their Medicaid patients as the Board may request whether or not they have given valid consents. If such a rule were issued and if a physician complied with a request for information about a patient who had not given a valid consent, the physician would not be in violation of the principles of medical ethics because they contain an exception to the prohibition against disclosure in situations required by law. To date no such rule has been issued. Instead Medicaid patients, before admission to a hospital, must sign a form authorizing release to their local Welfare Board of all information relating to the hospitalization. The Welfare Department has no comparable release form for use when a physician sees a Medicaid patient in his office rather than in the hospital. Therefore a physician may be faced with a request for information about a Medicaid patient whom the physician has seen in his office and who has never signed a consent for release of the information the physician obtained in his office. If the physician refuses to release the information until he receives a valid authorization from the patient and if the Welfare Board refuses to obtain such an authorization from the patient, the ethical physician will be faced with the alternative either of obtaining himself from the patient the necessary authorization or of foregoing payment for his services. For this reason some physicians require each Medicaid patient when he first becomes a patient to sign a form authorizing the physician to hand over to the Welfare Board all information it may require.

Even where patient authorization has been obtained, additional questions are often posed by the scope of the inquiry. Ideally, the party requesting patient information should limit his inquiry to those details which are necessary to process the claim or to carry out his statutory function and should not request extraneous information the disclosure of which might prove embarrassing to the patient. As desirable as that goal may be, however, it must be recognized that the physician is not in a position to make such value judgments and should try to avoid making them whenever possible. Therefore, the patient's written authorization should be so worded as to allow the physician to release any and all information acquired by him in the course of examination or treatment and should not contain any qualification or condition which might require interpretation.

Similar questions are presented by requests for autopsies and autopsy reports. All health insurance policies must, by state statute, contain a provision granting the insurer the right and opportunity to make an autopsy "where it is not forbidden by law." This provision has been interpreted by the courts to require a demand by the insurer for an autopsy and a consent to the autopsy by the decedent's next-of-kin. The courts have further held that the insurer may deny benefits if such consent is withheld. The Workmen's Compensation Act contains a similar provision. State law also empowers county medical examiners and coroners to conduct autopsies in cases of violent death or death under unusual or mysterious circumstances, and the consent of the next-of-kin is not required. The medical examiner or the coroner may also conduct autopsies where the body is to be disposed of by cremation or other irretrievable means or in the case of the death of an inmate of a public institution, but in these instances the examiner must obtain either a court order or the consent of the surviving spouse or other next-of-kin. Since the conduct of an autopsy does not involve a physician-patient relationship, it would seem to follow that the principle of confidentiality is also not involved—at least not in its usual sense. Where consent of the widow or next-of-kin is required, it relates not to the disclosure of information revealed by the autopsy but to the right to conduct the autopsy in the first place. Once such consent is given, the physician is free, without any further authorization, to make a full report directly to the party for whose benefit the autopsy was made, *i.e.,* the insurance company or the county attorney, as the case may be.

Frequently autopsies are performed at the request of the next-of-kin or at the suggestion of the physician and with the consent of the next-of-kin. In most such cases, the deceased's estate or the next-of-kin will be charged for the autopsy. At least in cases where such a charge has been made, it appears that the person charged is entitled to a copy of the autopsy report.

Meetings

MSMA-MINNPAC Workshop

All Minnesota physicians and their wives interested in learning how they can increase medicine's influence in government are cordially invited to attend the first statewide MSMA/MINNPAC Public Affairs Workshop. The workshop is scheduled for Saturday, June 15, at the Radisson South Hotel in Bloomington, beginning at 9:30 a.m.

Congressmen, legislators, campaign management experts and other opinion-makers will inform you on issues and show you how to meet the increasing threat of government control of medical practice through political action. The registration fee of $10.00 includes luncheon. A program and registration form have been mailed to all Minnesota physicians and Woman's Auxiliary members. Pre-registration is encouraged. For further information, you may call MSMA at (612) 222-6366 or MINNPAC at (612) 336-6262.

High-Risk Pregnancies and Newborns Course

A two-day continuing education course on the subject of high-risk pregnancies and newborns is being presented at the request of physicians in northern Minnesota, June 28-29, 1974 at Quadna Mountain Lodge in Hill City, Minnesota.

The course is sponsored jointly by the Office of Continuing Medical Education and the National Foundation March of Dimes. Physicians whose practice includes these problems and nurses in the obstetric services in northern Minnesota hospitals are invited to attend. The course fee is $10.00. Further information contact:

Continuing Medical Education
1350 Mayo Memorial Building, Box 293
University of Minnesota
Minneapolis, Minnesota 55455
Phone: (612) 373-5454

Great physicians cannot all attend,
But some they visit, and to some they send.[*]

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[*] John Dryden, "The Hind and the Panther," ll. 909-910. 1687.

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Special Article

The Intrauterine Device

Contraceptive or Abortifacient?

THOMAS W. HILGERS, M.D.*

In light of current, accepted medical definitions of contraception, abortifacient, pregnancy, conception, and abortion,[1][2][3] the conclusion is that the primary action of the IUD must be classed as abortifacient.

INTERAUTERINE DEVICES (IUD) have an antifertility effect in every animal species tested. However, the mechanism through which such devices nterrupt the reproductive process seems to differ from one species to another.[1] It is not possible, therefore, to explain the mode of action in a manner that applies to all species studied. Furthermore, the differences in the anatomic and physiologic features of the reproductive system among animals make it difficult, if not impossible, to arrive at conclusions applicable to man yet based on studies of animals.[1] Although much research has been done on rats, rodents, rabbits, sheep, cows, and monkeys, it can only give certain clues of what to study in the human being. Any *direct* comparison between man and animals, therefore, s always of questionable relevance.

This discussion will be devoted to the extensive research that has been conducted in human bengs. As far as is known, no such review has ever been undertaken. Animal studies will be mentioned only when they seem particularly pertinent from a historical or scientific viewpoint.

Historical Introduction

Intrauterine devices have allegedly been in use o control fertility for more than 2,000 years.[2] For centuries, Arabian and Turkish camel drivers have inserted a small round stone, the size of a kidney bean, into the uterus of their saddle animals prior to a desert trip.[3] This has been said to repulse the advances of the male as if the female were pregnant.[4]

In 1909, Richter,[5] a German physician, first described the insertion of two or three strands of silkworm gut into the human uterus for birth prevention. His work went almost unnoticed.

In 1916, Dickinson[6] predicted that a simple, safe, and effective intrauterine device eventually would be adopted for purposes of birth control.

It was not until 1928, however, that the modern history of IUDs began. In that year, Gräfenberg,[7] a Berlin physician, reported on the insertion of silkworm gut stars, later to be supplanted by silkworm gut rolled into rings and bound with silver wire, as a means of intrauterine birth control. In 1929, he[8] reported on 2,000 insertions of his new device. He found a 1.6% failure rate and no signs of the device causing inflammation of the uterus. His results were significant since later reports of similar results became the springboard for the present use of IUDs.

An early enthusiast of this method of birth control, Leunbach,[9] of Copenhagen, inserted 175 rings over an eight-month period in 1929 and 1930. His enthusiasm waned, however, and he rejected the device as harmful and unreliable.[10]

Later Haire,[11] a follower of Gräfenberg, " . . . used the ring for a number of years, but 'because of the possibility that it may be an unsuitable method, in a considerable portion of women' he did not recommend it in his last article." The condemnation of the Gräfenberg ring by both Haire and Leunbach is noteworthy from a historical perspective because they had actual experience with the device. Tietze[12] wrote that condemnation came only from those who had never had such experience.

In 1940, Kimbrough and Tompkins[13] stated on the basis of "dozens of unfavorable reports, the use of an intrauterine foreign body . . . as a 'contraceptive' is regarded as dangerous practice if not malpractice." This was the state of things until 1959 when the present history of the IUD began.

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*Resident in Obstetrics and Gynecology, Mayo Graduate School f Medicine, (University of Minnesota), Rochester, Minnesota.

Presented at a seminar in obstetrics and gynecology on October . 1972. This paper prepared under the supervision of members f the faculty of the Mayo Graduate School of Medicine.

See editorial, page 477.

Send reprint requests to: Dr. Hilgers, ℅ Section of Publication, Mayo Clinic, Rochester, Mn. 55901.

At the Second International Conference on Intrauterine Contraception,[4] the mechanism of action of the IUD was candidly discussed. Delegates to the conference expressed concern over the label "abortifacient" being given the IUD, since it would be detrimental in promotion of the device in underdeveloped countries like Pakistan, where abortion is strongly opposed.[14] Discussion aimed at redefining pregnancy to begin at implantation began as a result of this concern.

Later, a scientific group of the World Health Organization (WHO) gave careful consideration to the proper name for these devices.[15] After considering such names as "intrauterine foreign body" (IUFB), "intrauterine contraceptive device" (IUCD), and "intrauterine device" (IUD), they unanimously accepted the name "intrauterine device" (IUD) with the recommendation that it be universally used in the medical literature. Most articles in the literature, written primarily through grants from the Ford Foundation and the Population Council, have ignored this recommendation and continued to use intrauterine contraceptive device. This rhetorical ploy is in direct contradiction to the mounting scientific evidence that the principal mode of action of the IUD as a "contraceptive device" is not the prevention of conception but, rather, the destruction of the human blastocyst prior to implantation.[16-28]

Action of the IUD

Intrauterine devices used in humans are generally composed of stainless steel or mixtures of polyethylene and barium sulfate.[4] The barium is added to make them radiopaque. Those being fashioned from plastic tubing can, as a result, be stretched into linear form and threaded into a Teflon tube. This catheterlike tube, with the bore of a soda straw, can be passed through the cervical canal just beyond the internal os; a plunger is then inserted to force the device into the uterine cavity. Since moulded plastic has "memory," the device can be reshaped into its original form after being discharged into the uterus. Today, well over 70 different models of IUDs are available[29] and they are being used by more than 10 million women.[16]

Other substances have been explored for use within the uterus to prevent pregnancy (e.g., copper and zinc). However, since these are not being readily used and are not yet licensed by the FDA, this review will be limited to the so-called inert IUDs (i.e., IUDs made of substances like plastic or stainless steel). However, as pointed out by this review, these substances are far from inert.

Effects on Menstrual Cycle and Ovulation

Most investigators agree that the IUD does not interfere with or inhibit the process of ovulation.[30-32] It has been shown also that the menstrual cycle is normal in length in women with IUDs.[33] This finding has been confirmed by endometrial biopsies[15,34-35] and visualization of corpora lutea at laparotomy, as well as by histochemical studies of the ovaries.[1]

Faucher et al.[31] noted that the postovulatory phase of the menstrual cycle was shortened in four of six patients studied and that the urinary pregnanediol was decreased in all six patients.[31] This could indicate impaired function of the corpus luteum and might implicate a luteolytic function to the IUD. If this were true, it might also implicate a role of prostaglandins in the mechanism of action of the IUD. Such a theoretical possibility has been mentioned[36] but as yet it has not been investigated. If such a process occurs, it would disturb the precise balance that is necessary for implantation.

Chronic Endouterine Infection

The possibility that chronic endouterine infection may play a role in the mechanism through which the IUD works has been investigated. Microscopic changes in the uterine lining, previously thought to be associated with chronic infection (chronic endometritis), have been reported to occur in varying degrees. A Japanese study reported 74% of patients wearing IUDs had signs of acute inflammation while only 19% revealed signs of chronic inflammation.[37]

Most American studies have focused on the incidence of a chronic inflammatory process in response to the IUD and these results indicate that 13 to 28% of women with IUDs have chronic endometritis.[35,38-39] One study from Taiwan placed the incidence as low as 1.7%.[37]

In a study of 200 patients Willson et al.[35] found that the presence of the IUD did not significantly alter the bacterial flora of the endometrial cavity. Mishell, et al.[40-41] found some cultures to be positive immediately after insertion of the device, but all of the endometrial cavities examined one month later were sterile.

The inflammatory reaction observed in about 20% of patients is not thought to result from infection but rather from a reaction of the endometrial lining to the chronic presence of a foreign body.[34] In any event, the endometrial lining in these patients is altered appreciably from the normal and it is conceivable that this disturbance may prevent the blastocyst from implanting.[42]

The Role of the Fallopian Tube

The role of the muscular activity of the fallopian tube has also been studied extensively although inadequately. In the normal, nonpregnant woman without an IUD, the muscular activity of the fallopian tube tends to be low in the preovulatory phase of the menstrual cycle.[43] After ovulation, the tubal peristaltic activity tends to increase while the uterus is quiescent. When the corpus luteum regresses, the tubal activity evolves into a typical menstrual pattern with outbursts of increased activity occurring at short intervals.[43] It is due to this diversity of effects that transportation of the blastocyst by tubal peristalsis is accomplished while the uterus rests.[43]

In 1965, when Mastroianni and Rosseau[44] reported that the presence of the IUD in superovulated *Macaca mulatta* monkeys was associated with rapid discharge of the ova from the tube to the uterus, the thought that IUDs in some way abnormally increased the muscular activity of the fallopian tubes became the commonest theory of how the IUD functions. Mastroianni and Rosseau gave monkeys gonadotropins so that they would ovulate at a predictably higher rate. Shortly thereafter, Kelly and Marston[45] reported that the transport of ova through the fallopian tubes of normally cycling rhesus monkeys was not affected by the presence of a foreign body in the uterus. It seems that Mastroianni and Rosseau's technique of giving their monkeys gonadotropins stimulated the tubal activity that they originally reported. In 1967, Mastroianni et al.[46] repeated their study in normally cycling monkeys without exogenous gonadotropin stimulation. They obtained the same results as Kelly and Marston and disbanded the idea that increased tubal activity was the prime mechanism by which the IUD exerted its effects.

In 1964, Siegler and Hellman[47] reported the cases of three patients on whom they conducted uterotubal insufflation after two months' use of an IUD. Only two of these patients were in the postovulatory phase of the menstrual cycle and their results indicated that no mechanical obstruction of the tubes existed. This series was much too small to permit any decisive conclusions regarding tubal physiology in the presence of the IUD.

Ishihama et al.[48] reported a similar investigation of 30 patients before and during insertion of the IUD. They found no remarkable difference in tubal activity between the two groups. They also reported their findings on tubal transport of a radiopaque dye that had been inserted into the tube and then observed via cinesalpingography. In their opinion the presence of the IUD did not strongly influence the muscular contractions of the fallopian tube.

In 1970, Makhlouf and Abdel-Salam[49] reported their studies of uterotubal insufflation in 100 women 5 days after menstruation. They found that the strength of tubal contraction was increased significantly over and above that of the control group in 96% of patients and that, in accord with this, the number of peristaltic waves was increased in 88% of their patients with IUDs. These changes persisted and actually increased the longer the IUD was in place. This was a well-controlled study, but it was done on women during the fifth day after menstruation or during the preovulatory phase, and these times are not applicable to the mechanism of action of the IUD.

In 1971, Kamal[50] reported his results on uterotubal insufflation in 50 patients, some of whom had had an IUD inserted for two to three years. He found definite impairment in uterotubal function presenting as spasm of the uterotubal junction or the isthmic portion of the tube. These changes returned to normal after the IUD was removed, which indicated that the IUD was the cause. Unfortunately, no mention was made of the time during the menstrual cycle when these observations were obtained.

While the specifics of tubal physiology in the presence of the IUD are still somewhat undefined, the work of Noyes et al.[51] describes the tubes and the action of the IUD. In an exhaustive search for ova in the human uterus and tubes, they recovered 11 eggs from 92 patients fitted with IUDs and only 12 from 161 women without IUDs.[51] This difference was not significant on chi-square analysis. It would appear that the tubal transport of eggs is not appreciably affected by the presence of an IUD.

The Role of the Myometrium

In the preovulatory phase of the menstrual cycle in the nonpregnant woman without the IUD, the muscular activity of the uterus tends to increase progressively with a period of stabilization just prior to ovulation.[43] Shortly after ovulation, there is a period of two to five days of uterine quiescence. During this time, implantation is possible and if it occurs, uterine quiescence is maintained by the corpus luteum of pregnancy.[43] If implantation does not occur, then uterine activity evolves progressively into the pattern of exaggerated muscular activity which is typical at the time of menstruation.[43]

The action of the uterine musculature in the presence of the IUD is considerably clearer than that of the fallopian tube. Johnson et al.[52] reported on 32 patients in whom they measured intrauterine pressures by the open-end catheter technique of Hendricks. This study had many drawbacks and their conclusion that no increase in uterine muscular activity occurs in the presence of the IUD is highly questionable in view of later reports.

In 1967, Bengtsson and Moawad[53] reported on a well-controlled series using Hendricks' technique. They found that in women with IUDs, prelaborlike uterine contractions begin four to five days after ovulation and progress to full laborlike contractions during the menstrual period. This activity is clearly abnormal and coincides with the transport and implantation of the blastocyst. They felt that this may play a part in the mechanism of action of the IUD.

Using a totally different technique, Behrman and Burchfield[54] reported in 1968 and Behrman et al.[55] reported in 1969 that, after ovulation, the uterus entered a period of complete quiescence lasting until 24 hours before the beginning of the next menstrual cycle. The differences between their results and the results of Bengtsson and Moawad[53] probably were due to the differences in the sensitivity of the two techniques. The transducer IUDs used by Behrman et a probably responded to only local changes muscle activity, while the catheter system Bengtsson and Moawad measured changes the cavitary pressure produced by the enti uterine musculature.[56]

In 1970, Moawad and Bengtsson reported the long-term effects of the IUD on uteri musculature.[57] In women who had been usi the device for at least three years, they agai found prelaborlike contractions beginning 4 5 days after ovulation. These were not encou tered in patients who were not wearing IUDs.

These studies have now been confirmed the Japanese[58] who also found prelaborlike co tractions in the postovulatory phase in patien with IUDs.

Serr et al.[59] found increased electric activity the uterine musculature during the postovulator phase in patients with IUDs. This activity, whic probably indicates increased uterine muscle ac tivity, was not seen in controls.

The evidence seems to be strongly in favo of some significantly increased uterine muscl activity in patients with IUDs during the tim when implantation would occur. This disturbanc may indeed lend itself to an interference of th implantation process.

Effects of Intrauterine Devices

On Sperm Migration

In 1964, Malkani and Sujan[60] did hysterec tomies on four patients who had been wearin IUDs for 10 days. All had had coitus the evenin before the operation. In all four patients, *activ* sperm were found around the IUD and in th fallopian tubes. Morgenstern et al.[61] corroborate these findings in a similar study of 13 women These patients, however, had been wearing th IUD considerably longer than the group of four Morgenstern et al. concluded that the chronic presence of an IUD does not prevent transport o spermatozoa to the sight of fertilization in th fallopian tubes. They did find a low sperm concentration in the tubes, but concluded that this i similar to what is expected in women withou IUDs.

Brown and Allen[62] artificially inseminated 1 patients, six with IUDs and six without, a few hours before hysterectomy. In all 12 patients active sperm were found in the fallopian tubes

They concluded, as did the other investigators, hat the presence of an IUD does not prevent he ascent of sperm to the sight of fertilization. Kesserü-Koos[63] also observed this pattern of sperm migration and no one has described conrary results.

On Fertilization

There is no evidence that the IUD consistently prevents fertilization. On the other hand, it seems ikely that fertilization occurs with normal or near normal frequency in the presence of the UD.[23] Noyes et al.[51,64-65] recovered a fertilized egg in the pronuclear stage from the right tube of a patient wearing an IUD who had had coitus two days prior to hysterectomy. This, in conjunction with the numerous intrauterine pregnancies that have been observed in the presence of an IUD Table 1), proves that conception can indeed occur.

Virkar[83] reported the case of a woman who had intercourse with the IUD in place. Shortly afterward, she had the IUD removed and an implanted pregnancy ensued. He stated that "this case nicely brought out the fact that ovulation and fertilization are not interfered with, but it is the process of implantation that is affected by an intra-uterine device." Other investigators[53] have reported the same observation.

It has been observed that the incidence of tubal pregnancy in a given population of women wearing IUDs may be somewhat less than one might anticipate;[84] however, the number of intrauterine pregnancies is, by comparison, greatly decreased. This fact suggests that the primary action of the IUD is at the uterine level.[27] If the process of fertilization were inhibited, an equal decrease in the number of tubal pregnancies might be expected. Since this is not the case, we can only surmise that fertilization takes place

TABLE 1
Results of 18 Studies of Patients With IUDS

Investigator	Year reported	Device used	Woman-months	Total pregnancies, IUD in situ	Spontaneous abortions	Ectopic pregnancies
Webster[66]	1971	Loop Saf-t-coil	3,190	4	2	1
Doyle et al.[67]	1970	Loop Spiral Coil	16,992	18 (5)*	3	0
Kullander[68]	1970	Spiral	1,716	4†	2	2
Vaughn and Dominguez[69]	1970	Saf-t-coil	Not stated	11	3	2
Solish and Majzlin[70]	1969	Spring	12,408	14	5	0
Ylöstalo et al.[71]	1969	Loop	1,902	9† (3)*	4	1
Horne and Scott[72]	1969	Loop Spiral	7,714	4†	2	1
Hall[73]	1968	Loop	21,350	53	23	4
Bolognese et al.[74]	1968	Bow Loop	18,848	44	5	0
McCammon[75]	1967	Bow	4,303	8	2	0
Cheatham et al.[76]	1967	Saf-t-coil	2,460	4 (1)*	3	0
Ringrose[77]	1967	Loop	10,640	16	4	2
Wajntraub[78]	1967	Ring	12,921	41	12	2
Blott and Radcliffe[79]	1966	Spiral	Not stated	7 (3)*	3	0
Lippes[80]	1966	Loop	21,909	23 (2)*	3	4
Willson et al.[35]	1965	Spiral	5,606	6	Not stated	3
Jessen et al.[81]	1963	Ring	1,252	5	2	0
Hall and Stone[82]	1962	Ring	6,396	2	0	1
Total			151,481‡	273 (14)*	78	23
Percent of total pregnancies					28.6%	8.4%
Combined percentages					37.0%	

*Number in parentheses indicate pregnancies in progress. The number is included in the total number.

†Additional pregnancies terminated by legal abortion. The numbers were not included in the total number because the outcome was unpredictable.

‡Total woman-months is greater than is shown because the numbers were not stated in two studies. Blott and Radcliffe[79] alone reported 1,884.

regularly and that the primary action is a post-conception, intrauterine one.

On the basis of direct intrauterine observation with the glass fiber hysteroscope in 55 patients wearing IUDs, Sakurabayashi et al.[24] concluded that the "fertilized ovum" was rapidly expelled from the uterine cavity. They observed that if the IUD was fitted well into the upper part of the uterine cavity no uterine implantation occurred although implantation was observed in the fallopian tube. Only when the IUD had displaced itself to the lower portion of the uterine cavity was implantation observed, and then only in the upper portion of the uterine cavity. This most unusual study seems to implicate a directly mechanical component to the mode of action of the IUD. This would seem likely in view of the observation[85] that the efficacy of a given IUD is directly proportional to its size and surface area.

Marston, Kelly, and Eckstein[23] found that, in monkeys, there was no difference between control and IUD study groups in the rate of occurrence of fertilization. The fact that fertilization was not disturbed in the presence of an IUD established that transport of the sperm was adequate and its capacitation was not hindered. They did find that fertilized eggs entered the uterus normally and once the eggs were in the uterine lumen they seemed to undergo rapid degeneration. This study is thought to be of particular importance because of the close anatomic, physiologic, and phylogenetic relation between monkeys and human beings.

Of Phagocytosis

In 1968, Virkar and Kelkar[86] first reported the existence of large numbers of active, multinucleated histiocytes in a study of 10 loopal smears.

In the same year, Israel,[87] also from India, reported a much larger series of 228 loopal smears in which she found only 55 containing multinucleated histiocytes. She also studied 65 endometrial aspiration smears taken immediately after removal of the IUD. None of these smears revealed multinucleated histiocytes. The majority of her patients were long-term users of the IUD.

In 1970 attention was called again to these phagocytic cells in a study of 37 loopal smears.[88-90] Sagiroglu and Sagiroglu noted that these cells were numerous and most of them were small and monocytic shortly after insertion of the IUD. Only after the IUD was present for longer periods did they note the larger, multinucleated cells.[88] Contrary to Israel's report, this was a consisten finding. They[88] also noted some phagocytosis o sperm. Some workers have interpreted this to b *the* mode of *"contraceptive"* action of the IUD However, the Sagiroglus also noted the "collective phagocytosis" of a giant material (though to be an ova or blastocyst) by the macrophages This finding, it seems, was most significant because they outlined as follows the ways the thought the macrophages created a hostile environment mainly for the fertilized ova.[88,91]

(1) With the presence of the IUD surrounde by millions of macrophages in the endometria cavity, the fertilized ova will not find hospitalit but hostility. (2) Macrophages, like biologi foam, cover the surface of the endometrium an isolate it from the blastocyst, thus preventing implantation. (3) When a fertilized ovum, as a gian foreign body, enters the endometrial cavity, th macrophages actively move on and isolate it fro the endometrium by a firm phagocytic siege. (4 Macrophages liberate an enzyme, protease. Th protease content of uterine fluid is increased twofold in the presence of the IUD. This is significan since the enzyme protease is a powerful lyti agent. The zona pellucida, the insulator an protective membrane of the ova, and then th blastocyst may be dissolved or degenerated b this enzyme. (5) Spermatozoa are also foreig bodies. In the presence of IUDs, the millions o macrophages may incapacitate some of them.

It has been shown that the primary cell typ in the *endometrial aspirate* of women with IUD is the neutrophil and not the macrophage.[27,9] Moyer and Mishell[27] think this indicates tha neutrophils are more diffusely distributed throughout the uterine cavity while the macrophages ar more adherent to the plastic IUD.

This intrauterine cellular reaction, which i evoked by the IUD, has been observed in all animal species.[16,87,92,93] Segal[16] stated, however, tha it is " . . . inadequate to create a spermotoxi environment but sufficient to prevent nidatio of normal blastocysts arriving on schedule, fro the oviducts." This is supported by the fact, a Moyer and Mishell[27] pointed out, that the cellular degeneration products of neutrophils an macrophages are "injurious to the unimplante embryo."

On Sperm Capacitation

Rosado et al.[94] observed a significantly increased concentration of calcium in the human endometrium of females wearing an IUD. They hypothesized that this may inhibit the capacitation process. Interestingly enough, these changes were observed in biopsy samples of the endometrium and therefore do not reflect the environment through which the sperm traverse to meet the ovum.

Kar and co-workers[95] have observed a similar increase in the calcium concentration in the endometrium of monkeys. Since it has been shown that capacitation is unaffected in the monkey,[23] one can assume that this calcium plays no significant role.

On the Endometrium

Results of studies on the endometrium with the IUD in place have been somewhat confusing and contradictory, perhaps because the material for study in the majority of cases was obtained from endometrial biopsy. This presents a major source of error in sampling because biopsies from a given site may not reflect the pattern of the endometrium as a whole; also, it is a blind procedure and one cannot be certain of the actual source of the specimen.[38]

Nonetheless, agreement is general that the IUD causes transient inflammation, with increased vascularity, some hemorrhage, and edema of the area of the endometrium that is in direct contact with the IUD.[17,18,34,35,39,96-99] In conjunction with this, it has shown that in some cases the IUD imbeds itself deeply or even buries itself in the endometrium. This area underlying the IUD shows evidence of pressure atrophy with compression and fibrosis.[34,98-102]

Many studies have been conducted to determine if the IUD in any way interferes with the normal synchrony. Some reports have indicated that there is no phase discrepancy in the presence of the IUD.[39,102] Many more investigators, using light microscopy, have reported a delay in the histologic maturation of the endometrium. They have found a preovulatory type of endometrium in the postovulatory period.[17,19,20,35,37,96,99,103,104] These changes seem to be particularly obvious in that area of the endometrium that is in close contact with the IUD.[19,99]

Wynn,[17,18] using the electron microscope, described changes in the ultrastructure of the endometrium which would indicate premature maturation. He found ultrastructural changes that were characteristic of those found several days later in the normal endometrium. He found a well-developed nucleolar channel system in epithelial nuclei in about 20% of preovulatory endometria, and predecidual changes in about 25% of specimens as early as 19 to 20 days. The synchrony, furthermore, often affected the stroma more than the epithelium.[18,101] Tamada et al.,[19] Japan, found similar results. Wynn and Sawaragi[101] stated that while they have interpreted their findings as a premature ultrastructural development, the alternative explanation would be retardation of histologic development. In either case, the evidence strongly suggests a disturbance in the synchrony of the endometrial and ovarian development that is normally required for implantation.[101]

On the Endometrial Fluid

The fluid or exudate that lies within the endometrial cavity surrounding the IUD makes up the milieu to which the blastocyst must enter. The biochemistry of this fluid is interesting.

The volume of the fluid is greatly increased in women fitted with an IUD, and especially those who have symptoms such as pain, discharge, or bleeding after its insertion.[32,105] This alone has been thought to be an impediment to blastocyst implantation.[105]

The pH of the fluid has been found to be decreased in one study[106] and unaltered in another.[21]

Kar et al.[21] consistently found large increases in the protein and nonprotein nitrogen concentration in IUD-fitted women irrespective of the stage of the menstrual cycle. The nonprotein nitrogen was primarily urea.[107,108] In general, these increases were thought to lead to an increase in osmotic pressure of the fluid rendering the milieu unfit for survival of the preimplantation blastocyst.[108] More specifically, urea is known to be disruptive to proteins, and excessive quantities of urea in the uterine fluid of women fitted with the IUD are almost certainly detrimental to the viability of the preimplantation blastocyst.[107]

Further biochemical changes also have been detected. Persistence of positive staining of the mucopolysaccharides of the ground substance with alcian blue up to day 20 to 24 of the cycle represents a failure of their depolymerization and this may decrease the receptivity of the endometrium to the blastocyst.[22,102]

When the three sugars—hexose, hexosamine and hexuronic acid—were studied, the results suggested that the IUD shifted the normal metabolic pattern of the endometrial mucosubstances. This may indicate a suppressive effect of the IUD on glycogen biosynthesis. This, too, is important in the antifertility action of the IUD.[109,110]

In a classic study of the biochemistry of the human endometrium, Joshi and Sujan-Tejuja,[111] from India, conducted quantitative assays on a large number of women with and without the IUD in order to establish basic cyclical patterns. They studied the quantitative differences in deoxyribonucleic acid (DNA), ribonucleic acid (RNA), tissue protein, alkaline phosphatase, and acid phosphatase.

The normal changes in concentration of RNA, DNA, and total protein are considered to be indicators of the action of estrogen and progesterone on the growth of the endometrium.[111] A comparison of these growth-activity indicators revealed that endometrial growth during the preovulatory and early postovulatory phases is actually stimulated by the presence of the IUD. Moreover, the peak concentration of RNA in the endometrium, which normally is not attained until day 16 to 20, actually was reached during days nine to 13 in the presence of the IUD, indicating an acceleration of growth. Higher concentrations of RNA and total protein in the endometrium of women using an IUD were found to be maintained even during days 21 to 24 when the growth activity of the normal endometrium is signficantly suppressed.[111]

Alkaline phosphatase and acid phosphatase activity also showed an increase. The increase in alkaline phosphatase activity probably reflects the participation of this enzyme in tissue growth.[111] The increase in acid phosphatase, a hydrolytic enzyme, was thought to represent an increase in lysosome function.[111] Lysosomes generally are considered to participate in intracellular and extracellular digestive processes.

Miscellaneous Effects

Some investigators have detected a prolonged or elevated secretion of the pituitary hormone oxytocin[112] while others have noted elevated blood levels of this same hormone in women who use IUDs.[113] This may indicate some systemic effect of the IUD as opposed to a completely local effect, but the actual significance of these findings still is not well understood.

Implantation in the Presence of the IUD

In any analysis of the IUD in which an attem is made to reach conclusions on either its co traceptive or its abortifacient nature or both, o must look carefully at those cases in which i plantation is known to occur in the presence the IUD. The outcome of these pregnancies of considerable significance.

Table 1 is a list of the individual and cumul tive experiences of 18 different investigators r ported in the medical literature. These studi were randomly selected. The only selective criteri were the accuracy with which the investigat reported the total number of pregnancies, th number of spontaneous abortions, and the num ber of ectopic pregnancies that occurred wit the IUD *known to be in place.*

In more than 151,000 woman-months of us there were 273 pregnancies with the IUD know to be in situ. Fourteen of these were still i progress at the time the author reported hi findings, but were here assumed to have gon full-term. Of these 273 pregnancies, 78 (28.6% ended in spontaneous abortion and 23 (8.4% ended in ectopic pregnancies. Therefore, a tota of 37.0% of all these pregnancies ended in feta loss.

This percentage of "fetal wastage" is signifi cantly higher than in women not wearing IUDs The normal incidence of spontaneous abortio is thought to be at least 15% of all pregnancie between the fourth and 20th weeks of gestation[114-116] (Table 2). The incidence of ectopi gestation in the white, middle class populatio of the United States is approximately 0.3% (1:330) and in the medically indigent, it is n higher than 1.0% (1:100).[117] It is the contentio of this analysis that the substantial and only difference between these two groups is the presenc of the IUD and, therefore, the increase in feta loss is directly attributable to the presence o the IUD.

TABLE 2
The Risk of Spontaneous Abortion in Pregnant Women

Investigator	Year	Percentage o spontaneous abortions
Warburton and Fraser[114]	1964	15
Erhardt[115]	1963	18
Tietze[116]	1953	14

Others have found similar results but have not taken this direction of thought. Their own data, however, substantiate this claim. Tietze and Lewit,[118] reporting on 782 uterine pregnancies in more than 261,689 woman-months of use, found that 41% or 542 pregnancies with the device known to be in situ ended in abortion. Perkin[119] reported that 36.4% of pregnancies occurring with the device in situ ended in abortion. (The number of pregnancies was not stated in this report, but it represented a substantial experience of 85,782 woman-months of use.)

Both of these reports stated that their data do not indicate the incidence of *induced* abortion. However, of the 240 pregnancies that occurred in Tietze and Lewit's series[118] in which the device was *not recovered*, only 33% ended in abortion. And in Perkin's study,[119] only 25.8% of those in which the presence of the device was "unlikely" aborted. Given a *distinct* separation into two groups, one with IUD and one without, the latter should serve as an inbuilt control series, for the pregnancies would be no less distressful than the ones with the IUD in place and the pressures to artificially abort would be the same.

In the simultaneous presence of an IUD and an implanted pregnancy, one can expect that in *at least* 10% of all pregnancies, spontaneous abortion will develop because of the mere presence of the device. However, the percentage may be and most likely is considerably higher than that. The *absence* of the device was never substantiated in either Tietze and Lewit's or Perkin's series and, therefore, an untold number may have aborted as the result of the hidden presence of an IUD. One must also take into account the tubal pregnancies (8.4%) that result in de facto fetal destruction. This increase in tubal gestation has been reported by others[25,84,120] as well.

In support of this concept, Tischler and Kraus[121] reported a case of spontaneous abortion in which the IUD had entangled itself in the umbilical cord and was thought to be the cause of fetal death.

In reality, the thought that a mechanical object in the uterus may be a cause of spontaneous abortion is nothing new in medicine. The presence of a naturally occurring mechanical obstacle, such as a submucous myoma, has been known to be a cause of habitual spontaneous abortion.[117]

In addition to all of this, if an IUD is inserted into an already pregnant uterus, it has been shown to cause an extremely high rate of spontaneous abortion.[73,122] If an IUD is removed from an already pregnant uterus, there is a substantial increase in the rate of spontaneous abortion.[72] Many such abortions have been reported.[72,73,122]

Summary and Conclusions

The IUD provokes many unnautral effects on the female reproductive system. These effects, working in unison, undoubtedly contribute to its ultimate action.

The IUD does not interfere significantly with the menstrual cycle, with ovulation, or with sperm migration. This appears well settled. There seems to be little question that active sperm, in adequate numbers, do reach the fallopian tubes where fertilization normally takes place. No evidence at the present time suggests that fertilization itself is prevented consistently. On the contrary, all available evidence strongly supports the concept that fertilization occurs at normal or near normal frequency.

Present knowledge indicates that the mechanism of action of the IUD is focused in the uterus. The effects exerted by the IUD on the endometrium, on myometrial activity, and on the intrauterine biochemical and biological milieu are destructive in nature, and under these conditions, the preimplantation blastocyst is unable to survive.

The number of live-born babies with IUDs implanted in their placentas disprove that the IUD always destroys the blastocyst. At the same time, one cannot say that fertilization always occurs, for certainly one could make a case for occasional prevention of conception. Nevertheless, given today's knowledge, it is evident that the IUD exerts its birth-preventative effects primarily through the destruction, at a uterine level, of the preimplantation blastocyst. The IUD, in the small number of cases in which implantation is allowed to occur in its presence, is a frequent initiator of the abortive process and, as a result, well-developed fetuses are aborted.

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Asymptomatic Gonorrhea

A Report of 2,128 Screenings in Rural Minnesota and a Review of the Literature

DAVID W. HILFIKER, B.A.,* MICHAEL A. BESS, B.S.,* AND
CHARLES S. MAHAN, M.D.†

The incidence of gonorrhea among clinically non-suspect women who present themselves to rural primary physicians in Minnesota was less than 0.13% in this study of 2,042 such women. Among those under 26, the incidence was less than 0.34% in 714 clinically non-suspect women. The low incidence in this population seems to mitigate against the routine screening of asymptomatic rural females in Minnesota.

FROM 1971 TO 1972, THE NUMBER of reported cases of gonorrhea in the United States increased from 624,371 to 718,401. In the same period, the number in Minnesota increased from 6,221 to 8,347 (37%).[1,2] The actual numbers occurring annually are undoubtedly much higher. In 1968 a survey of 135,000 private physicians indicated that 89% of treated cases of gonorrhea were not reported.[3] Thus, it may be approximated that in 1972, 6.5 million people in the United States were treated for gonorrhea.

The reported incidence of gonorrhea varies widely according to age, sex, race, geographic distribution, reporting source, urbanization, and season.[4,5,6,7] The incidence is highest in the 15-24 year old age group. The greatest increase over the past two years has been in the 15-19 age group. This increase in reported cases may be a product of increased diagnosis and case reporting brought about by venereal disease (VD) programs and legislation directed at teen-agers.[4,5] The incidence in non-whites tends to be greater than in whites; the difference, while probably real,[8] is believed to result in part from more complete case reporting among minority groups who, for economic reasons, go to public clinics.[4,5,7]

Variations in the reported incidence among states are subject to wide differences in case finding activity, availability of public clinics, and attack rates. In 1972 Minnesota was fifteenth lowest with a reported incidence of 197.3 per 100,000. A low of 71.0 per 100,000 was reported from Maine. South Carolina was highest with a rate of 818.1 per 100,000.[5] The number of cases reported from sources other than private physicians has consistently been higher than from private physicians. In 1970 almost three times as many cases were reported by other than private physicians.[6]

Urbanization is an important factor in the incidence of gonorrhea. From 1969 to 1970, the reported case rate for cities of over 200,000 increased from 610.3 to 662.6 per 100,000 (8.5% increase) while the incidence for cities of 50,000 to 200,000 increased from 289.4 to 336.9 per 100,000 (16.4% increase). Over the same period, the incidence for smaller towns and rural areas increased from 84.6 to 98.7 per 100,000 (16.7% increase).[4,6] These reported case rates are probably influenced by the urban availability of non-private health facilities and their use by highly mobile rural populations.

The evidence which points to a large and epidemiologically significant population of asymptomatic female carriers has prompted recommendations for the routine screening of all females who present for pelvic examination.[9,10,11] The diagnostic method of choice has clearly been shown to be culture.[12,13,14] Currently available Thayer-Martin medium has been shown to be capable of detecting well over 90% of those infected.[12,15,16] Smear examinations are 30-40%

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less sensitive than culture.[15,17]

Many physicians in Minnesota maintain that the incidence of gonorrhea in rural communities does not approach state and national levels and have not initiated screening programs. Until recently the unavailability of a reliable and convenient transport medium has also been a deterrent to screening. Culture using Thayer-Martin culture medium (TM) requires inoculation, immediate placement in a 3% CO_2 atmosphere (usually candle-jar technique) and incubation at 35° to 36° C. on the same day as inoculation.[15] However Transgrow medium (TG) is currently available for both transport and culture. The medium appears to be as sensitive as Thayer-Martin and capable of maintaining viability of the gonococcus for three full days.[18] This length of time is greater than for any other previously available transport media. Recent clinical investigations have, however, shown Transgrow to be somewhat inferior to enriched Thayer-Martin medium for rate of positive culture detection when postal transportation is used. A decline in rate of recovery has been noted in proportion to the number of days in postal transit.[19,20]

To determine the incidence of asymptomatic gonorrhea in females in rural Minnesota, a series of females presenting to rural primary physicians for pelvic examination was investigated.

Method

Ten third-year medical students (participating in the year long Rural Physicians Associate Program) and their preceptors volunteered to participate in the study. All were based in Minnesota towns of less than 12,000 population. With assistance from the Minnesota State Department of Health, all clinics were provided with adequate quantities of Transgrow medium to culture all women undergoing pelvic examination in each of the clinics. All participants were provided with instructions regarding the methods for obtaining, incubating, and transporting cultures.

> "Culture all women for whom a pelvic examination is performed, regardless of age or presenting complaint. Moisten the speculum with water; do not use any other lubricant. Remove cervical mucus with a cotton ball held in ring forceps. Insert a sterile cotton-tipped swab in the endocervical canal and move freely from side to side; allow several seconds for absorption of organisms onto the swab. Remove the cap of the Transgrow bottle only when ready to inoculate the medium and maintain the bottle in an upright position to minimize CO_2 loss. Soak up all excess moisture in the bottle with the specimen swab and then roll the swab back and forth across the medium, starting at the bottom of the bottle. Incubate the Transgrow bottle in an upright position at 35-37°C. for 16-18 hours before mailing. Mail bottles in the containers provided by the Health Department."

For each woman cultured, the following information was coded: Age, marital status, whether the patient suspected she had gonorrhea at the time of the examination, whether the patient believed she had been exposed to a male infected with gonorrhea, the presence or absence of symptoms (defined here as dysuria, vaginal pain, and/or lower abdominal symptoms), birth control methods used, and culture result. Culture specimens were all mailed to the Minnesota State Department of Health.

Results

A total of 2,218 endocervical cultures were obtained during November 1972 to March 1973 from ten different clinics in rural Minnesota. Of the 2,128 screenings carried out, five yielded culture results positive for *Neisseria Gonorrhoeae*. The incidence of positive cultures in symptomatic and asymptomatic women is shown in Table 1. Of 2,059 women who were asymptomatic, only three had positive cultures. The yield of various groupings of patients according to clinical characteristics is shown in Table 2. When patients without

TABLE 1
Screening Results According to Symptoms

	Number	Negative Culture	Positive Culture	"No Growth" Culture	"Overgrown" Culture
Asymptomatic	2,059	3	757	1,281	18
Symptomatic	69	2	30	37	0
Totals	2,128	5	787	1,318	18

TABLE 2
Subgroups of Patients Screened

		Culture Positive	
Characteristic	Number*	Number	Percent
Suspected Gonorrhea	22	3	13.6
Known Exposure to Gonorrhea	10	2	20.0
Dysuria, Vaginal Pain, and/or Lower Abdominal Symptoms	73	2	2.7
No Symptoms, Contact or Suspicions	2,043	2	0.096

*Patients assigned to more than one subgroup when appropriate.

symptoms, as well as those without any other characteristics to raise clinical suspicion are considered, the number of non-suspect patients with positive cultures is two out of 2,043 patients.

If each of the patients with positive culture is considered individually (Table 3), the incidence of gonorrhea in clinically non-suspect women is reduced further. In patient E, vaginal discharge alone was present. With this clinical characteristic of note then, the number of positive cultures in clinically non-suspect patients is reduced to one, giving a 20% non-suspect carrier rate among females with gonorrhea. The presence or absence of vaginal discharge as a symptom was not reported for all patients since this is a common occurrence and is commonly associated with frequently occurring, relatively benign lower genital ract infections.[21] The results for clinically suspect and non-suspect women, as well as age breakdown, are summarized in Table 4.

Of the cultures taken, 18 (0.89%) were reported as "overgrown" and 1,318 (62%) were eported as "no growth". Excluding both of these ypes of cultures from the study gives a populaion of 792 patients with a detected gonorrhea incidence of 0.63% (5 positive cultures). In the clinically non-suspect group, the incidence is 0.13% when all ages are considered and 0.34% for the under 26 age group, when "overgrown" and "no growth" cultures are excluded.

Discussion

The increase in gonorrhea to epidemic proportions has been due to a number of factors. Changes in the Neisseria organism itself with a decreased virulence (and, thus, symptoms) and increased antibiotic resistance have been noted. An increasingly mobile population, changes in sexual attitudes and behavior, and possible changes in sexual practices have all been cited as contributing to the increase.[22] Asymptomatic gonorrhea, particularly in the female, is undoubtedly an important factor in the continued rising incidence.[21,18,23,12]

Asymptomatic Carriers

Gonorrhea in the male is usually symptomatic and offers little difficulty in diagnosis. Asymptomatic gonorrhea in males does, however, exist and may be present in up to 10% of exposed males, depending on the population studied.[24,25,26]

TABLE 3
Culture Positive Patients

Patient	Age	Marital Status	Contraceptive Methods	Patient Suspected Gonorrhea?	Known Exposure to Gonorrhea?	Symptoms
A	25	Divorced	Oral	Yes	Yes	No
B	19	Married	None	Yes	No	Yes (dysuria, vaginal pain)
C	19	Single	IUD	Yes	Yes	Yes (dysuria, lower abdominal symptoms)
D	21	Married	None	No	No	No
E	24	Single	Oral	No	No	No*

*Vaginal discharge present.

TABLE 4
Age Groupings of Clinically Suspect and Non-Suspect Patients

	Age Group	Number	Culture Positive	Culture Negative	"No Growth" Culture	"Overgrown" Culture
Clinically Suspect	Under 26	52	4	22	26	0
	Over 26	34	0	16	18	0
	Total	86	4	38	44	0
Clinically Non-Suspect	Under 26	714	1	292	415	6
	Over 26	1,328	0	457	859	12
	Total	2,042	1	749	1,274	18

It is estimated that 50-90% of females who have gonorrhea have no symptoms.[4,9,27] These figures are emphasized by the work of Waters and Roulston: Using Thayer-Martin (TM) culture medium, 3,375 general hospital prenatal patients were screened with the detection of 89 cases; 64 (72%) of which were associated with no symptoms.[28] Additional evidence for a high rate of asymptomatic females is taken from the disproportionately higher number of male gonorrhea case reports.[5]

While it has been suggested that the percentage of asymptomatic females found to be infected with gonorrhea may be falsely elevated due to the presence of non-pathogenic strains, there is strong evidence to the contrary.[29,30] Brown and associates[3] successfully infected male volunteers with both pure cultures and swabs taken from asymptomatic females. Pariser has recently cited evidence agains females harboring non-pathogenic strains.[9,31] The significance of the asymptomatic female as a reservoir for dissemination of gonorrhea has been questioned. Hughes and Davies discovered no cases of gonorrhea after screening 725 asymptomatic females in London, England and concluded that if the regular partner of an asymptomatic female has not developed the disease, then she has no fear of being a carrier.[32] This may

TABLE 5

Review of Asymptomatic Gonorrhea in Females

Investigator	Population Characteristics	Number of Patients	Incidence of Gonorrhea	Incidence of Asymptomatic Gonorrhea
Rees and Hamlett Liverpool 1972 (Prospective)	Urban "Slum clearance area residents"	100*	2 (2.0%)	0
	Pregnant	219†	0	0
Waters and Roulston Winnipeg 1964-67 (Retrospective)	Urban "Public service of obstetrics and gynecology" patients	3,375	89 (2.7%)	61 (1.8%)
Cassie and Stevenson Glasgow 1973 (Prospective)	Urban "Social classes 4 and 5" Pregnant	1,000	2 (0.2%)	0
Kraus and Yen Cleveland 1965-66 (Prospective)	Urban "Clinic population" Pregnant (cultured during ninth month)	1,309	75 (5.7%)	75 (5.7%)
Zachler, et al. Chicago 1968-70 (Prospective)	Urban "Lower socioeconomic areas" "Pregnant women, marriage applicants, volunteers for family planning service, and patients seeking VD examinations"	107,301	8,027 (7.5%)	8,027 (7.5%)
Hart Atlanta 1971 (Prospective)	Urban "Patients of private obstetricians and gynecologists" "Upper middle-income group"	231	6 (2.6%)	5 (2.2%)
Cave, et al. New York 1969 (Prospective)	"Large urban voluntary hospital"	875	72 (8.2%)	20 (2.3%)
Charles, et al. Chicago 1967-69 (Prospective)	Urban "Lower socioeconomic area residents" Pregnant	2,160	158 (7.3%)	158 (7.3%)
Venereal Disease Branch, CDC United States July-Sept. 1972 (Prospective)	"Gonorrhea screening programs" VD Clinics	89,097	17,676 (19.8%)	17,676 (19.8%)
	Non VD Clinics	482,133	19,371 (4.0%)	19,371 (4.0%)
	Private Physicians	98,603	3,708 (3.8%)	3,708 (3.8%)
	Total	571,230	37,047 (6.5%)	37,047 (6.5%)

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*With symptoms.
†Without symptoms but "high risk" (ie, single and pregnant, admitting to extramarital intercourse, etc.).

not be true considering the lack of a regular male partner in the high risk population; the frequent occurrence of spontaneous cure in the asymptomatic female; the lack of 100% male inoculation per exposure; and the increasing occurrence of asymptomatic infections in the male.[4,22,24,25,33]

The low incidence of gonorrhea in our patient population probably reflects the tendency toward lower rates among patients seen by private physicians[36,39] (Table 5), as well as the lower rates of gonorrhea in rural areas.[4] Seasonal variations in the reported incidence of gonorrhea have occurred in national statistics with marked regularity over the past fifteen years. The peak each year occurs in the July-September quarter with the low point each year being the January-March quarter.[6] Even though the current study lacked uniform seasonal collection distribution, the variation between high and low points annually is only 15%; clearly not great enough to significantly affect the results which were obtained.

Transport Media Problems

Media overgrowth with spreading organisms (usually Proteus) has been reported for TM media at a rate of 0.65-5.8% of the cultures inoculated.[15,36] On surveys using TM, the usual practice has been to exclude from the population all "overgrowth" results since an exact determination of the presence or absence of gonococcal organisms is not possible.[40,36] In view of this, it seems reasonable to repeat the culture whenever possible on patients who have cultures reported as "overgrown".

The causes and implications of the "no growth" results in our study (using TG with pre-incubation) are not clear. When steps are taken to assure positive culture recovery rates compatible with TM (i.e. pre-incubation and less than one day transportation[20]), there is no reason to assume that "no growth" results should be viewed any differently for TG than TM. Hart, of the United States Center for Disease Control, considered "no growth" on TM to be negative results.[36] "No growth" may be due simply to the presence in both media of relatively high concentrations of inhibitors for other than Neisseria organisms. In the present study, the climate conditions during postal transportation of specimens (ambient temperatures from +60° F. to –30° F.) and the transit time involved for postal transportation (always greater than one day) may be partly responsible for the abnormally high rate of "no growth". If so, clinicians may not be able to rely on "no growth" results and may, in our opinion, have to treat clinically and epidemiologically suspect patients without positive culture confirmation of diagnosis.

Gonorrhea in Rural Minnesota

The incidence of gonorrhea of 0.34% in clinically non-suspect members of the high risk age group (under 26 years) is from 6 to 22 times lower than that found by other investigators (1.8-7.5%) for urban North American populations screened by culture techniques other than TG.[21,23,28,36,34,35] The results in our study, however, are similar to findings from studies carried out in Liverpool and Glasgow[37,38] (Table 5).

No conclusions can be drawn from this study concerning the actual incidence of gonorrhea among rural women. Rural women suspecting venereal disease may often travel to urban areas for diagnosis and treatment to assure anonymity. The existence of the study was not common knowledge in the participating communities; therefore, there is no reason to suspect that the presence of the study created a less representative population. The incidences noted above, however, refer only to that population of women visiting rural physicians for pelvic examination.

Given the low incidence of gonorrhea in clinically non-suspect females presenting to rural physicians as detected by this investigation, it does not seem advisable for rural physicians to culture all women or even those in the high risk age group. Because of the ease (less than 30 seconds added to pelvic examination in most cases) and low cost (all materials are available through the Minnesota State Health Department) of screening, however, certain conditions may warrant routine screenings. If a rural physician has some reason to suspect that his community differs significantly from the cross section of communities included in the study, screenings should probably be carried out. The screening of all pregnant women also seems to be a worthwhile endeavor since the incidence of gonorrheal ophthalmia neonatorum is increasing.[11] Detection by screening during the ninth month of pregnancy may reveal some cases which might be missed by earlier culturing either due to a failure of the organism to grow or a late gestational onset of infection.[35]

Acknowledgment

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We are also indebted to many medical students and physicians for their assistance in the screening program.

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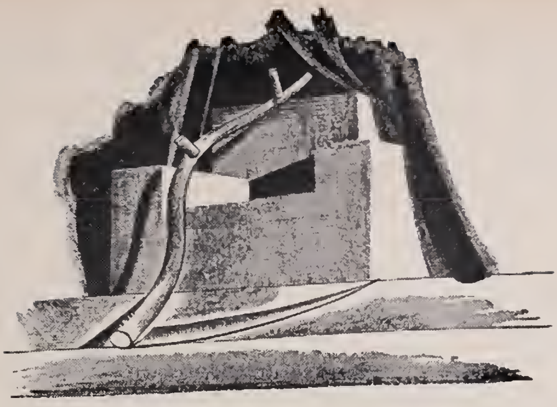

In Memoriam

JOHN A. McINTYRE, M.D.

Dr. John A. McIntyre, 83, Owatonna surgeon, died March 1. He was a graduate of Cornell College and Harvard Medical School.

Dr. McIntyre had practiced medicine for 50 years and had served as County Health Officer for 18 years. He was a member of the Academy of General Practitioners, Steele County Medical Society and the Minnesota Academy of General Practitioners and a Life and 50 Club Member of the Minnesota State Medical Association.

He is survived by his wife, Margaret, four sons, John, William, James and Philip.

JAMES (JACOB) A. POLZAK, M.D.

Dr. James Polzak, 77, Roseville urologist, died March 26. He was a graduate of the University of Minnesota Medical School and had been chief of urology for many years at the Northern Pacific Hospital in St. Paul.

In addition to being a member of the American Medical Association and the Hennepin County Medical Society, Dr. Polzak was a Life Member of the Minneota State Medical Association and was to be named to he Fifty Year Club at its annual meeting in Duluth.

He is survived by his wife, Irma, and sons, James and Robert.

REUBEN M. ROSENWALD, M.D.

Dr. Reuben M. Rosenwald, 85, Minneapolis surgeon, died February 22. He had been on the staffs of St. Barnabas and Maturnity Hospitals.

Dr. Rosenwald was a member of the Hennepin County Medical Society and the American Medical Association and an Associate and 50 Club Member of the Minnesota State Medical Association.

WARNER G. WORKMAN, M.D.

Dr. Warner G. Workman, 86, died March 8. He had practiced medicine in Tracy for 52 years. A graduate of the University of Minnesota Medical School, Dr. Workman was made a Fellow of the American College of Surgeons in 1926. After his retirement, Dr. Workman spent more time with his favorite hobbies, horses and sailing, and in the affairs of the community.

He was a member of the Lyon-Lincoln County Medical Society and the American Medical Association and was a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Workman is survived by his daughter, Virginia, and son, David.

TRUMAN A. HEDEMARK, M.D.

Dr. Truman A. Hedemark, 77, Ortonville physician. died March 24. He was a graduate of the St. Louis University Medical School and before coming to Ortonville had practiced in Revillo, South Dakota, and Thief River Falls, Minnesota.

He was a member of the West Central County Medical Society and the American Medical Association, a former president of the Whetstone Valley District Medical Society and a Life Member of the Minnesota State Medical Association.

EDWARD K. ENDRESS, M.D.

Dr. Edward K. Endress, 75, St. Paul surgeon, died February 26. Born in St. Paul and educated at the University of Minnesota Medical School, Dr. Endress had practiced in St. Paul all of his career.

He was a member of the Ramsey County Medical Society and the American Medical Association and a Life Member of the Minnesota State Medical Association. He was to have been honored this year as a Fifty Year Member.

Dr. Endress is survived by two daughters, Joan, and Jean.

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(Continued on page 512)

Fixing Cytology Smears

We pathologists have a fixation about cytology smears.

Now that you mention it, we have five fixations.

The *first fixation* applies to cervical and vaginal smears. First and foremost is this: such smears ought to be fixed promptly, i.e. within seconds after they are taken.

There are several ways of achieving this end: 1) by dipping the slide (or slides) into a nearby solution of 95% acetone; 2) by spraying the slide with Spraycyte (Clay-Adams Co.); or 3) by spraying the slide with Aquanet—an inexpensive aerosol for holding women's and men's hair in place. We lean towards the latter because it's effective and inexpensive (50¢ for a 16 ounce can). Also many prominent laboratories use it.

The *second fixation* concerns body fluids: pleural effusions, ascitic fluid, breast aspirations, and sputums. These fluids have a way of degenerating rapidly unless the fluid is immediately refrigerated or delivered fast without being exposed to the vagaries of the U.S. Mail.

The *third fixation* concerns Gravlee Jet Washings. As you probably know, this is a new technique whereby you irrigate the uterine cavity with saline to obtain material for cytology smears. This washing should be left in saline without fixation, refrigerated immediately, and delivered with speed.

The *fourth fixation* has to do with your solutions. You may not be aware of it, but if 95% ethanol or 90% acetone solutions are left uncapped the solutions take moisture out of the atmosphere. A water-logged fixative does not preserve cellular detail well.

The *fifth* (and last) *fixation* relates to the pathologist's problem with information. When he's interpreting a smear, he likes to know the patient's age, sex, history, previous treatment (if any), and the suspected problem. If he has this information, he can do a better job. Besides, the information makes the quest for cells more satisfying intellectually. And that's partly what it's all about. You wouldn't want pathologists to have fixed ideas, would you?

Richard L. Reece, M.D.
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*Cesare Lombroso, The Man of Genius, Part I.

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Book Reviews

THE POWER AND THE FRAILTY. Gene Hamberger. MacMillan, $4.95. 138 pages.

Hamberger is Professor of Medicine at the University of Paris.

Only after one has read a few pages dealing with some of the philosophical thoughts of Professor Hamberger, then the title of the book takes on greater significance.

The book deals principally with the tremendous power that has been accumulated in the field of Medicine, but it bewails the frailty of medical men to deal with that power.

Certainly no one man in Medicine would ever be able to encompass the entire field and its numerous ramifications. In order to profit fully from the advances of Medicine, a new type of medical practice may be in the process of being developed.

One cannot decry the need for continued and even more limited specialization, but for the sake of the patient, even if a specialist eventually becomes necessary, the general practitioner, he believes, must be so well trained and his scientific prestige so outstanding that he can continue to oversee the medical or surgical treatment from beginning to end. The practitioner must be expert enough to engage in effective dialogue within a specialized center.

Things* have happened so fast in the field of Medicine that the world is still dazed and muddle-headed like a drunken reveler who has riotously experienced a bewildering avalanche of unexpected events. The urgent need for lucidity is so pressing that it seems certain that it will soon come about. However, though Medicine strives for universal benefit to all mankind, the individuality and the creative genius of a dissatisfied, unhappy man must not be destroyed by bureaucratic dictum.

Dr. Hamberger clearly indicates that there are so many wonderful things in the field of Medicine that are not understood except by a few, that it would be a pity if one could not believe in God and the universal knowledge that awaits us in the future.

I heartily recommend this book for serious enjoyment.

Carl O. Rice, M.D., Ph.D.
Editor Emeritus

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*Computerization of medicine, gene alteration, the control of personality with new drugs, and the surgical alteration of criminal tendencies.

CORRELATIVE NEUROANATOMY AND FUNCTIONAL NEUROLOGY, 15th Ed. Joseph G. Chusid, Lange Medical Publications, Los Altos, 1973. 430 pages, $8.50.

Once a text has achieved the status of a 15th edition and has been reprinted in many foreign tongues, a reviewer is tempted merely to add his accolades. Chusid's book on correlative neuroanatomy and functional neurology is such a book. The new edition follows the format of earlier editions and has sections on the anatomy of the central, peripheral and autonomic nervous system. Motor, sensory and reflex disturbances are outlined. A simplified analysis of higher cortical function deficits is also included. The major neurodiagnostic techniques are touched upon with brief statements on CSF, EEG, EMG, electrodiagnosis and radiology. Cystometry, neuroophthalmology and neurootology are not neglected and information is included in objective and projective psychometric tests. The book closes with a clinical section which covers congenital, vascular, infectious, traumatic, neoplastic, degenerative and metabolic derangements. Disorders associated with disturbed consciousness, e.g. epilepsy and narcolepsy are discussed and headaches, neuromuscular and psychiatric diseases are each dealt with in a chapter. The appendix has information on the neurological examination including tests appropriate for the neonate, a developmental scale and references to major standard texts of neurology.

All this is packed into just over 400 small pages. Chusid's ability to present such a wide array of material concisely is due to his exceptional talents in outlining a subject, his reliance on charts and his excellent drawings. Although allegedly written for the beginner, the material is too concentrated to be of great help to one really without a background in neurology. Rather, the book can be of most value to one already equipped with a firm foundation in this specialty. The experienced clinician can better pick his way through the material and fill in from his background omitted details. The book therefore is recommended for more advanced students who wish to enjoy a refresher course and review. The paperback binding helps keep the cost of this little classic down and allows its recommendation as a worthwhile addition to a personal library.

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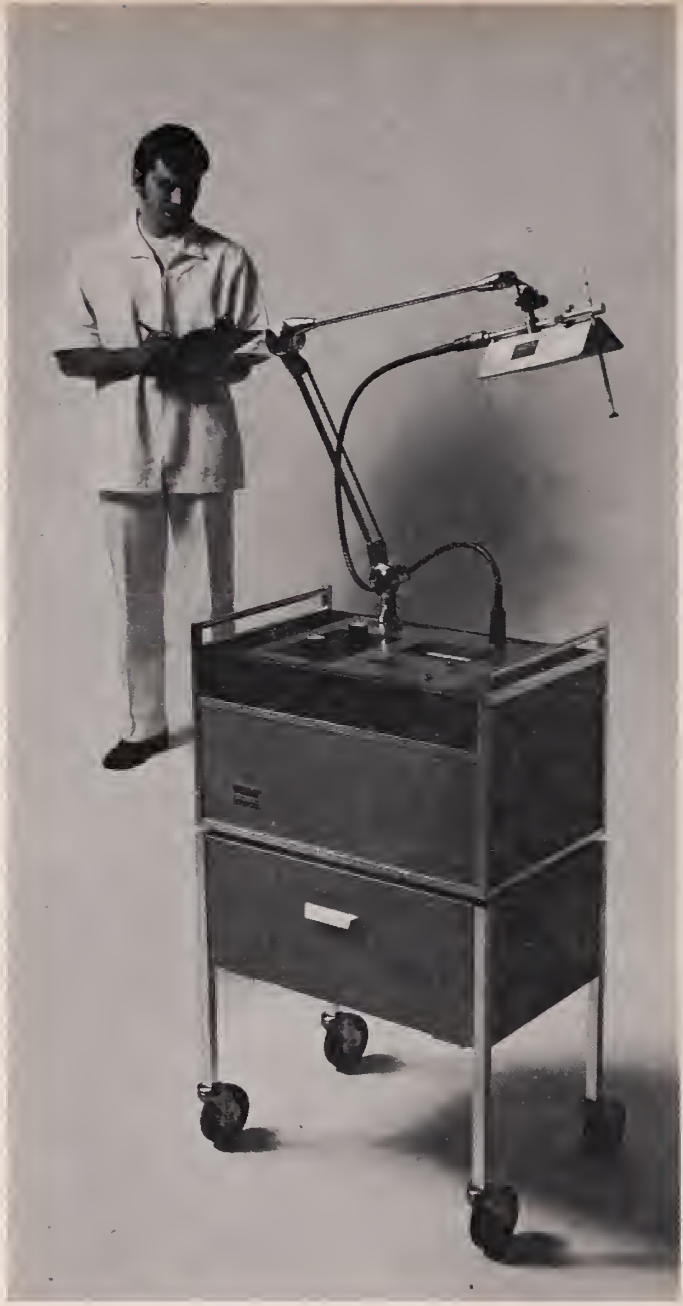

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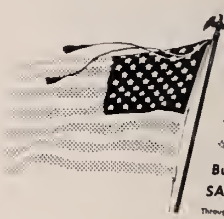

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The patient with asthma or allergy:
another type for Tylen
(acetaminophe

When the allergic patient has a condition requiring an analgesic, a new problem arises. "Idiosyncrasy to salicylates is not rare and is usually manifested by skin rashes and anaphylactoid reaction. Sensitivity to these drugs occurs more frequently in patients with asthma and allergy."[1] Moreover, the previous ingestion of aspirin without ill effects is no guarantee that subsequent use will not precipitate a severe reaction.[2]

TYLENOL (acetaminophen), on the other hand, presents little risk of allergic reaction, even in patients sensitive to aspirin,[3] making it the preferred analgesic for the allergic patient.

This is only one of several 'types for TYLENOL'—that is, patients who should avoid aspirin. Considering all of them, wouldn't it provide added safety (as well as added convenience) to recommend TYLENOL (acetaminophen) routinely for simple analgesia?

References: **1.** Modell, W., ed.: Drugs of Choice 1970-1971, St. Louis, The C. V. Mosby Company, 1970, p. 196. **2.** Goodman, L. S., and Gilman, A., ed.: The Pharmacologic Basis of Therapeutics, ed. 4, New York, The Macmillan Company, 1970, p. 327. **3.** Maslansky, L. Paper delivered at Fourth International Congress of Allergology, New York, Oct. 18, 1961: abstracted Excerpta Med. Internat. Congress Series, No. 42, p. 124.

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President's Letter

1776 and Now

"That to serve these rights [life, liberty, and the pursuit of happiness] governments are instituted among men deriving their just power from the consent of the governed."

Jefferson's words from the Declaration of Independence, written in another time, still ably state the source of power of a democratic government. The legislature derives its power from and is responsible to the people, a responsibility that is felt only if the people make their wishes known.

Physicians as a group are often vocal in their protests in the hospital staff room, or over coffee at the luncheon table. Aside from these sporadic outbursts which rarely attract the attention of legislators or officials in power, most physicians are politically inactive. Many would be hardpressed if forced to name their elected State representatives. Even more would be unable to recognize them. How can these legislators know your desires or obtain your consent unless you communicate with them?

An easy but effective way to express your views is through membership in MINNPAC (Minnesota Political Action Committee). MINNPAC dues moneys are used to support candidates, regardless of party, who are receptive to our arguments and who will consider our points of view.

Activities in a group such as MINNPAC are often more effective than individual activities. But personal contact with candidates through work on campaign committees by physicians and members of our families must not be discounted. Grass roots activity is needed: sending out campaign literature, donating funds, ringing doorbells. An extra pair of hands sometimes means more than money to an understaffed campaign.

You might ask if this activity is really necessary. During the last legislative session alone more than three hundred bills either directly or indirectly affecting medicine were introduced. Decisions basic to the future of medicine in this state are being made. Our participation in these decisions is vital to the preservation of quality medical practice. With legislative interest in the field of health at an unprecidented high, action taken in the next few legislative sessions may determine the nature and type of medical care in the future.

We have all seen that legislative action can be constructive. The development of the University of Minnesota Medical School is an excellent example. The Medical School faculty, responsible for this issue of MINNESOTA MEDICINE, and the University's educational program for students and practicing physicians deserve much of the credit for the generally high standards of medicine in this state.

Many changes in the present medical system are now being contemplated by the legislature. Independent status for allied medical personnel to the limits of their training is often suggested. The public utility approach with an area franchise of care awarded to centers or groups is being considered. Accompanying this would be a commission appointed by the legislature to establish charges. Such changes, if enacted, would inevitably affect the standards of medical practice.

If we are to insure the right of all to a healthy life, we must contribute to the decisions now being made in the legislature. The time has come for increased political awareness on the part of the medical profession.

Bernard Hall M.D.
President
Minnesota State Medical Association

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Opinion & Dialogue

Is there a need for a drug compendium?

Government Health Official

Henry E. Simmons, M.D.
Deputy Assistant Secretary for Health
Department of Health, Education and Welfare

A drug comp of the type I en would fill a defir need for the ing physician compendiur give him informatic essary fc a drug intelligently, and it w do so in a clear, concise, co venient, objective and balar fashion.

What a Compendium Should Contain

I believe the compend should inform the doctor wh drug will do, when he shoul for what type of patient, for long, in what dose, what ber his patient is likely to obtair risks involved, and cross-re with other drugs.

The information woulc based on the package inser have the same legal status. a complete compendium wi plete and current informati might even eliminate the ne

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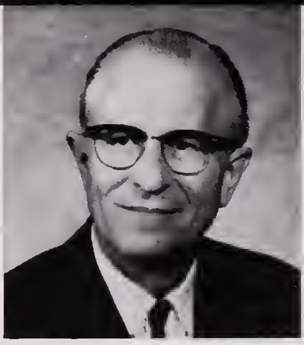
Maker of Medicine

Joseph F. Sadusk, Jr., M.D.
Warner-Lambert Company



A drug compendium, preferably compendia, shou believe, be private, not fede sponsorship. They should c comprehensive listings of d available for prescribing. Th should be single, legibly pri volumes of reasonable size, dated quarterly or semiann and completely revised eve

Function of a Compendium

A compendium shoulc nish the following informati drugs in the following order tions for use, side effects, a drug reactions, contraindic drug interactions, drug dos the dosage forms marketed prices should not be includ cause they vary so widely ar change rapidly.

No compendium shou forth drugs of choice or dis relative efficacy. Such ques must be left for the practici sician to decide, whether or basis of the medical literatu own clinical experience, ad colleagues, information su by manufacturers, and so o

Nor should a compen undertake to educate the d how to use drugs. Rather, it be a reference source desig marily to refresh his memo drugs he may not use regul

package insert in many in-
es. This would constitute a
antial saving for the manu-
rer.

By a complete compendium,
ot mean a volume of prohibi-
ze. You don't need a book
ibing 25,000 products with
ormous amount of repetition.
r, drugs should be arranged
ss. Mutually applicable infor-
n would be provided, along
rief discussions pinpointing
ences in specific drugs of
ass. Listings would be cross-
ed in a useful way.

**Available Documents as
es of Information**

xisting references such as
nd the AMA Drug Evaluation
viously useful but they are
plete. Either they are not
referenced by generic name
not group drugs with simi-
racteristics, or they do not
the available and legally
ted drugs. And some of
omitted may be very useful.

On the other hand, drugs made by more than one supplier, tetracycline for example, may be fully described a dozen times in the same book.

While perhaps PDR could be rearranged and cross-indexed with generics included, and while the AMA Drug Evaluation might also be modified and expanded, I am not sure that the end result would have all the attributes required for a useful compendium. At the same time, you would run the risk of amassing a voluminous and unwieldy tome.

Should Editorial Comments Accompany the Listings?

Subjective judgments, in my opinion, have no place in a compendium. However, if there is substantial evidence based on a sound body of science concerning relative efficacy of several drugs, certainly that information should be included. The committee of experts compiling and editing a particular section would also have to assess and indicate instances where a meaningful difference between drugs is pertinent.

Sponsorship, Compilation and Editing

Producing a book like this would undoubtedly be difficult and demanding. It would obviously take a great deal of talent and expertise, and would require a varied and experienced group, ranging from writers and editors to highly skilled clinicians and pharmacologists. Style, format and clarity of language would play an important part in determining the usefulness of the book. And it should be updated periodically and completely revised annually.

I have no opinion whether the government or the private sector should sponsor and/or finance the compendium. What is most important is that the compendium be an authoritative, objective and useful source of information for the doctor to have at hand as a ready reference.

d in no way imply control over
actitioner's prerogatives.

nother Compendium?

A practicable, single-volume
endium cannot, nor is it
sary to, include all drugs on
arket today. From my prac-
internal medicine for some
ars, my experience as a con-
t, and as a faculty member
or five medical schools, I
estimate that a doctor uses
0 to 35 drugs regularly. The
Physicians' Desk Reference,
ntally, contained about
entries.

As to whether there should be
ral compendium, in my opin-
stated earlier, the answer is
there should *not* be one. The
sal assumes that existing
endia are inadequate. We're
re of that at all. Whatever its
ections, the present drug
ation system in the U.S. is
multifaceted, pluralistic and
ive. Good compendia exist,
as other ample sources on
herapy, ranging from journal
ure through AMA Drug Evalu-
o company materials. Not
sicians may use such
s as often or as well as they
, but that is the fault of the
ot of the sources.

n any event, rather than produce another book, it makes much more sense to work on improving existing compendia, and perhaps they could, as knowledge advances, include more accumulated clinical data and experience, and more information on drug interactions and adverse reactions.

Implications of a Federal Compendium

Take a hard look at the implications of a federal compendium. It would have the force of law, virtually dictating what drugs to use and how to use them. In effect, it would be a regulatory document with legal or quasi-legal status, posing medical/legal problems similar to those the doctor may now encounter if and when he departs from the provisions of the package insert. A compendium under federal aegis would tend to restrict decisions on drug therapy to one orthodox level—a most dangerous trend for medicine.

New Compendium—A Medical Option

I detect no ground swell of initiative or support whatsoever for a federal compendium—or, for that matter, for a new compendium of any type. A 1969 PMA survey conducted by Opinion Research Corporation found that only 15 per cent of those physicians interviewed felt a new compendium was needed. And a large majority did not favor the involvement of the federal government if one were to be created, preferring instead a nongovernmental consortium.

Even if we come to a time when the medical profession itself opts for a new kind of compendium, it should be handled and financed, ideally, outside both government and industry. Final review and editorial authority could be delegated, say, to specialty bodies and medical societies—but above all, *not* the government.

Surely the health care system in the United States has far more vital matters to consider than the extensive cost and effort that would have to go into the preparation and maintenance of a new, monolithic compendium, and especially one bearing the imprimatur of the federal government.

Opinion & Dialogue

What is your opinion, doctor? We would welcome your comments.

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Masonic Memorial Hospital

A Special Cancer Center for the Study of Advanced Malignant Diseases

B. J. KENNEDY, M.D.*

The recognition by the Masons of Minnesota in 1955 of the needs of patients with cancer led to the creation of the Masonic Memorial Hospital as a Special Cancer Center for the care and study of patients with advanced malignant diseases. The hospital provides care, facilities, and equipment, as they relate to advanced cancer and allied chronic diseases. It provides physicians in training with experience in the problems of oncology, develops programs for training specialists in oncology, and aids in the development of the new specialty of Medical Oncology. The impact of the foresight of the Masons of Minnesota in the development of this unusual Special Cancer Center is noted in all Minnesota communities.

"BUILDING AS MASONS build—brick upon brick, stone upon stone—the members of the Masonic Fraternity of Minnesota created a hospital devoted to the care of those afflicted with cancer; they dedicated their work to God . . . in the face of a disease which now strikes a strange and nameless fear into the hearts of men, the Masons asserted their faith in the power of love to cast out fear, and in the power of men's mind to discover truth; this hospital, built on a foundation of faith, is not a place of desolation; it reflects the belief that fear cannot be without hope."[1]

The Masonic Memorial Hospital coordinated with the adjacent Veterans of Foreign Wars Cancer Research Center was established at the University of Minnesota Health Sciences Center for he study of advanced malignant diseases and has been designated by the National Cancer Institute as a Special Cancer Center. The hospital is a model for the demonstration of cancer teaching, esearch in advanced malignant diseases, and deection and management of patients with cancer. n this environment a positive, realistic approach oward the problems of advanced cancer prevails. Developmental efforts are directed toward `the biologic behavior of cancer, detection, new therpies, control and cure of advanced malignant diseases, rehabilitation, alleviation of suffering and care of the dying patient. The concern for adequate cancer facilities is part of the nationwide problem of caring for patients with chronic diseases.

Seeking a solution to the problem of terminal cancer, Masonic leaders meeting in 1955 stated: "We have an urgent need for hospital care for patients with cancer and other incurable diseases. These are the most neglected. Their tragedy involves both themselves and their families. What can members of the craft and of associated bodies do to supply leadership in filling this great need?"

A proposal to build a hospital at the University of Minnesota devoted to this problem was approved by the University Board of Regents. The full cost of the building was provided by the Masons of Minnesota. The hospital, an 80-bed, two story structure was completed and presented to the University of Minnesota in 1958. On September 17, 1960, the University of Minnesota conferred its highest honor, the Regents' Award, upon the Masons of Minnesota in special recognition of their qualities of benefaction, fidelity and leadership.

In 1963, to meet the additional space needs for patient care and research, the Minnesota Masons through the Masonic Memorial Hospital Fund, Inc., provided funds to build two additional floors to the Masonic Memorial Hospital, adding 40 beds. At a Victory Jubilee on April 19, 1966, the Masons presented the University of Minnesota with a solid gold check for $1,100,000. This

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*Professor of Medicine, Director of Medical Oncology and Masonic Professor of Oncology, University of Minnesota School f Medicine, Minneapolis, Minnesota.

Supported by research grants CA-08101, CA-05158, and CA-8832 from the National Cancer Institute of the United States ublic Health Service, the American Cancer Society, the Minesota Medical Foundation, the Leukemia Research Fund, Inc., f the University of Minnesota Foundation, the Masonic Memoal Hospital Fund, Inc., and private donors.

unique public relations vehicle depicting one aspect of the Minnesota Masonry's humanitarian efforts has been exhibited in the Chase Manhattan Money Museum, New York City.

The Masons of Minnesota charged the University of Minnesota with a statement of mission. To this charge, the University replied: "We hereby formally state that we do accept the charge given us by the Masons of Minnesota, acknowledging the greatest responsibilities it entails. Further, we pledge ourselves to the manifold task bequested to us: to do all in our power to make this hospital reflect the faith and sense of brotherhood shown here by the Masons of Minnesota; to care for those stricken with cancer . . . to further the fight against cancer; to join with our fellow scientists to find the cure for cancer."[2] In October, 1966 the National Cancer Institute designated the facility as a Special Cancer Center.

The Masons of Minnesota continued their program of fighting cancer by establishing a Masonic Professorship in Oncology at the University of Minnesota in 1970 and subsequently by providing support of research and teaching programs aimed to benefit the care of patients with cancer.

Clinical Experience

With the advent of modern medicine, people are living longer. In place of a brief illness and death a patient is often beset with chronic problems of heart disease, cancer, rheumatoid arthritis and other allied diseases. These problems created a need for a type of facility different from the acute hospital, emphasizing a shift towards direct nursing care. It was initially regarded that an increasing need for such facilities to provide nursing and medical care, that is less intense than an acute hospital but greater than a nursing home, could be provided in what is termed a "parahospital."[3] The Masonic Memorial Hospital was originally deemed to be less than a general hospital, but more than a nursing home, specifically designed for the care of patients with advanced cancer and other serious, chronic illnesses.

In the initial three years of operation of the Masonic Memorial Hospital, the facility proved adequate to meet these needs. Subsequently, the type of medical care available to patients with advanced malignant diseases altered, mainly due to advancements in chemical therapy. As a result, the intensity of medical care in the Masonic Memorial Hospital increased, placing greater demands upon the nursing services and requirin more extensive medical staff. Special diagnosti procedures were done more frequently. With th increased use of toxic chemotherapeutic agents protective isolation techniques had to be observed more often and close observation made fo reactions to the therapy. More nursing care wa required. Because of the incurable nature of th diseases, the patients require more emotional support and personal attention than acutely ill patients. As a result the hospital has become a full operational intensive medical unit. The improvements in the method of chemical therapy and th more rapid rehabilitation of new patients resulte in a decrease in the average length of stay fron 32 days to eight days, while the number of patient entering the institution increased (Figure 1).

With the decreased hospitalization period an the increased rehabilitation of patients, an increasing demand upon ambulatory services for the patient has resulted. The Masonic Research Clini was developed to meet the needs of pediatric an medical oncology patients. Since 1968 there ha been a rapid increase in the number of patien visits (Figure 2). Special nurses have been traine to meet the needs of the chemical therapy programs of advanced malignant diseases. Thes nurses and expansion of the post-graduate medica training program personnel and faculty, have me

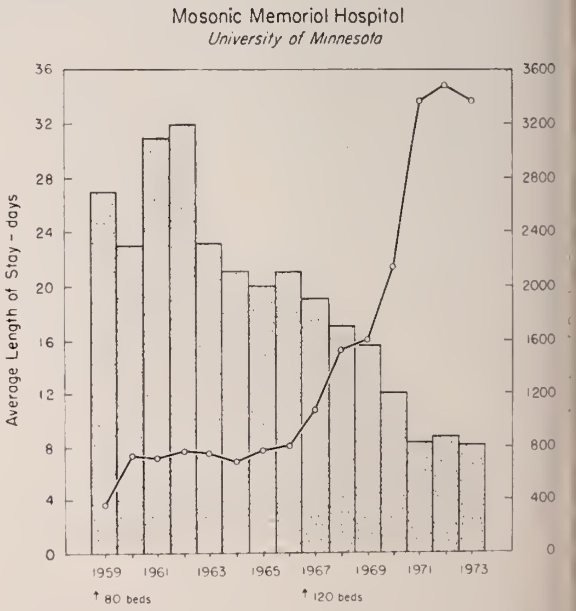

Fig. 1—Average length of hospitalization for patien in the Masonic Memorial Hospital and the number c discharges (black line). In 1967 the added beds resulte in increased admissions for neurological diseases whic were of short duration.

he professional demands required by the increasng ambulatory care load. It is projected that an ncrease in ambulatory care facilities will continue o be the major thrust of the future advancements n cancer medicine care.

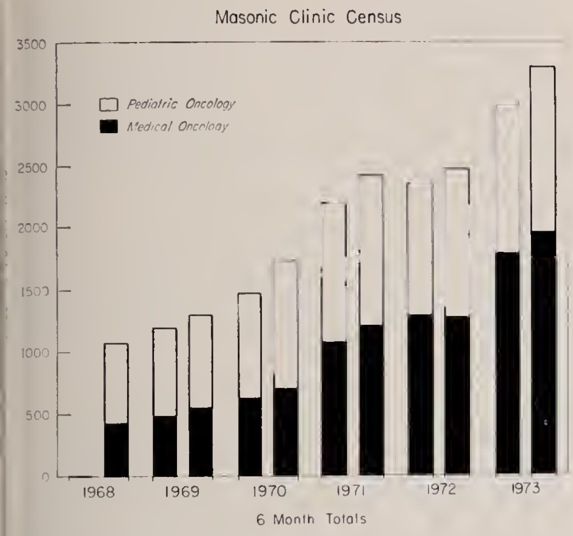

Fig. 2—Increasing number of Masonic Research Clinic isits. This does not reflect the oncology visits to other ollow-up clinics at the University Hospitals.

Nature of Patients

The original design of the Masonic Memorial lospital was to create a "terminal" facility, a rm that now is inappropriate in view of the ccomplishments and advances in the manageient of patients with advanced malignant diseases. urrently, a variety of patients are managed in ie Masonic Memorial Hospital:

1. Patients with recurrent or advanced maligant diseases who require evaluation and establshment of treatment programs that are then istituted by the family physician.
2. Patients with advanced malignant diseases iat require specific therapy administered in the ospital facility with subsequent maintenance proams in the clinic or at home. Such therapies ay be either routine or part of a research proam.
3. Patients specifically admitted for research irposes in instituting new therapies or study of lvanced malignant diseases.
4. Patients receiving radiotherapy who are too to be maintained on an ambulatory care basis.
5. Patients being prepared for therapeutic produres such as surgery.
6. Patients in convalescent states.
7. Patients who have had cancer and who develop illnesses that may or may not be related to the cancer.
8. Patients undergoing diagnostic evaluation of their illness.
9. In keeping with the initial intent of the Masons of Minnesota the hospital continues to provide care of patients in the dying phase of cancer. Domicillary care, however, is not provided beyond three months. In actuality, the dying patient constitutes a small percentage of the total patients now treated at the Masonic Memorial Hospital.

Patients admitted to the Masonic Memorial Hospital are informed of their diagnosis in order to conduct a positive and realistic program of cancer therapy. This is particularly true in areas where investigative agents are to be employed, in order to meet the federal regulations for use of investigative compounds. It has been the experience of this faculty that the patients who are properly informed of the presence of cancer are able to adjust to this knowledge, and with understanding of the disease, cope with the problems of cancer more appropriately.

Initially a community dining room was established with the plan that patients would eat their meals together. As a result considerable support was provided to the patients because of such socialization. A study evaluated the reaction of patients to the communal dining room and the effect of the cancer para-hospital setting on the patients.[4] The advantages of a total facility devoted to the care and complete truthfulness with cancer patients allowed inter-reactions between the staff and patients which are truly unique. The patient dining room, while of primary importance in the improvement of some patients, was considered as just one part of the total therapy afforded. While some patients benefit from socialization with others, still others profit more from a nursing staff which is unafraid to confront cancer. It has been strongly emphasized not to underestimate the capacity of the cancer patient to adapt to his condition.

No Cancer Present

A significant number of patients referred with a diagnosis of advanced malignant disease on evaluation were found to have no active cancer or no cancer at all. The signs and symptoms of other medical ailments simulated the symptoms of recurrent cancer. Because of the earlier presence of a malignancy, the new symptoms had been interpreted as due to a recurrence of the cancer. On evaluation and search for recurrent cancer, diagnosis of other diseases resulted; such as jaundice due to gall stones, weight loss due to thyrotoxicosis, fatigue due to infectious mononucleosis, osseous lesions due to hyperparathyroidism, hepatitis in a patient previously transfused at the time of surgical resection of a tumor, and multiple sclerosis instead of metastatic central nervous system disease. These instances emphasize that patients who have had cancer or patients with active cancer are susceptible to other medical illnesses and that a differential diagnosis must be considered for every new symptom or sign.

Teaching

The oncology services provide the medical student an early opportunity to learn about cancer, an opportunity not previously a part of the medical school curriculum.[5] The student acquires knowledge in handling the main entity, but he also learns the arts and skills of alleviating discomfort, bringing about improvement in performance and function, and providing purposeful continuity in care. He learns how to control pain, insomnia, constipation, diarrhea, nausea, and pruritus. He learns to relieve anxiety, anguish, depression, grief, and guilt in the patients and the relatives. He appreciates the role of religion.

The student sees the social and economic aspects of chronic illness as they affect the individual, the family, and the community. He learns to appreciate the significant contributions of other professionals such as social workers in the care of the chronically ill patient. He is faced with the constant realization that patients with advanced malignant diseases also develop other illnesses. Hence, the cancer patient provides a teaching resource for general medicine.

In internal medicine the Masonic Memorial Hospital acted as a pioneer in describing the role of the medical oncologist. In 1972 Medical Oncology became a recognized subspecialty of Internal Medicine.[6] There is a great demand by young physicians for fellowship training in this new subspecialty. The demands by the community for such trained physicians are overwhelming. Graduates of the existing program have become leaders in oncology programs elsewhere in the United States.

The Masonic Memorial Hospital operational policies for nursing are aimed at preserving t nurses' time for actual patient care, with attemp to limit administrative and clerical activities this profession. The skills developed have result in the evolution of the oncology nurse. Nurs are being trained for public health programs, sp cial hospital units for cancer patients, as well replacing local needs. The Masonic Memor Hospital provides a base for training clergy, occ pational therapists, physiotherapists, social wor ers, psychologists, and dietitians in the manag ment of patients with cancer.

Cancer Detection Center

The Cancer Detection Center was establish at the University of Minnesota in 1948. It mov into the Masonic Memorial Hospital in 196 From 1948 to 1969, 80,111 examinations we performed on 14,978 patients over the age of 4 Cancers detected and confirmed number 660, one cancer for each 23 patients.[7] The advantag of periodic examinations in asymptomatic patier have been demonstrated.

Clinical Research Center

An 11-bed Clinical Research Center was esta lished in the Masonic Memorial Hospital in 19 as part of a program of the National Institutes Health. Special problems studied have includ leukemia, cancer, diabetes, renal failure, and he disease.

Masonic Leukemia Treatment Center

A center for the treatment of acute and chror leukemia has been established at the Masonic M morial Hospital. Optimal treatment of acute le kemia requires an aggressive chemotherapeu approach, specialized professional personnel, t availability of blood cellular components and n crobiological resources. These factors constit the basis for a leukemia center. The Masonic Le kemia Treatment Center consists of four ma components:

The Adult Leukemia Treatment Service (Medical Oncology)

The immediate treatment of acute leukemia urgent. Vigorous induction chemotherapy is stituted. The Adult Acute Leukemia Treatm Service participates in the national cooperat Acute Leukemia Group B program.

ediatric Oncology

The management of children with acute leuke- ia is conducted on the inpatient service of the epartment of Pediatrics. The Pediatric Oncology ervice participates in the cooperative Childhood roup A programs.

eukapheresis Unit

The development of the cell separator (celltri- uge) has resulted in a safe and rapid method to rocess large quantities of whole blood in a closed, erile, continuous flow system.[8] The major clini- l uses are leukocyte collection for transfusion to atients with leukopenia, and leukocyte removal in e management of patients with chronic leukemia. The Leukapheresis Unit is a cooperative research program between the Blood Bank and the Medical Oncology Service.

The *Masonic Research Clinic*

This clinic was designed as an ambulatory treatment unit for patients requiring special cancer services. Because of the success of induction chemotherapy of children and adult patients with acute leukemia and success in solid tumor therapy, an increasing number of patients are managed in an ambulatory setting. Long-term maintenance programs are conducted in this clinic. Arrangements are made with the family physician to continue the maintenance programs in the home community.

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Polyposis of Colon, Osteomatosis, and Soft Tissue Tumors Syndrome

This syndrome consists of multiple polypi of the colon, cranial exostoses, and soft tissue tumors. It was first reported by Gardner and associates in 1951. A familial disorder, it was found in six members of a family group of 51 living persons; in addition, eight deceased family members were reported to have died of cancer of the colon or rectum. Each of the eight had subcutaneous tumors and six had osteomas. Gardner and associates concluded that the occurrence of these three abnormalities in a family group was probably due to a single defective gene with a dominant mode of inheritance.

Weiner and Cooper* later studied and treated three brothers with this unusual combination of abnormalities. Two of the patients were found to have adenocarcinoma of the rectum or colon in addition to multiple polyposis. A fourth brother, treated elsewhere, had multiple adenocarcinomas of the large intestine. Roentgenograms of the skull of this patient showed numerous exostoses. No soft tissue tumors similar to those found in the other three brothers were present. These writers believe that their patients comprise the second family group in which this syndrome has been observed. They expressed the belief that the bony changes may be the first manifestations and emphasized the frequency with which carcinoma of the colon develops. They also pointed out that these patients are prone to develop fibrous tissue tumors after surgical incisions.

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Hoeber Medical Division, Harper and Row, New York

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*Weiner R and Cooper P: New Engl J Med 253:795, 1955.

Acute Leukemia

Modern Management

CLARA D. BLOOMFIELD, M.D.*

MAJOR ADVANCES IN the treatment of acute leukemia have occurred since the first trials of chemotherapy by Farber in 1948.[1] The average survival for children with acute lymphoblastic leukemia prior to the introduction of effective chemotherapy was less than three months.[2] Today, when appropriately treated, the disease may be curable in 50% of children.[3] Ten years ago a 25% remission rate in adult acute granulocytic leukemia was exceptional. Today complete remissions in 40% of patients over 60 and in 87% of adults under 60 are being achieved.[4,5] The aim of treatment in acute leukemia has changed from palliation to cure.

These advances in the treatment of acute leukemia have greatly increased the physician's responsibility. The diagnosis of acute leukemia must be made promptly, and every patient offered the benefit of optimal therapy. Treatment of acute leukemia is a highly developed specialty and dependent upon extensive support facilities. Patients with acute leukemia should be referred to specialized centers for initial treatment and development of a long range therapeutic plan. Most patients now survive induction chemotherapy and return home from the specialty center. All physicians therefore should be able to administer maintenance antileukemic agents and recognize problems related to the disease and treatment. Delays in initiation of aggressive therapy or failure to recognize impending problems, once justified by "they all die anyway" is no longer medically acceptable.

Acute Lymphoblastic Leukemia (ALL)

Diagnosis and Classification

Acute lymphoblastic leukemia is a disease cha acterized by progressive malignant infiltration the bone marrow and lymphatic organs by lyr phoblasts or immature lymphocytes. General the "stem cell" or undifferentiated leukemias a also included in this group although they have much worse prognosis. ALL constitutes the gre majority of childhood acute leukemia but only minority of adult acute leukemia.

Recently there has been increased interest the subdivision of ALL into morphologic class based on the nature of the predominant maligna cell. Several groups have shown that survival ar response to therapy differ for the various su classes.[6-8] Mathé and his coworkers[6] have divid ALL into four cytologic varieties: prolymph blastic, macrolymphoblastic, microlymphoblast and prolymphocytic. They find better surviv using only moderately intensive chemotherap for patients with the microlymphoblastic and pr lymphocytic varieties. Similarly, Pantazopoul and Sinks[7] have subclassified ALL into thr groups according to the proportion of macrolyr phoblasts in the original pretreatment marro Children with less than 10% macrolymphobla have a prognosis superior to those with great numbers of macrolymphoblasts.

For many years at the University of Minneso we have subclassified ALL into two major cyt logic types.[8] Our designation is acute lymphocyt leukemia when the majority of leukemic cells a lymphoblasts; the designation subacute lymphoc ic leukemia is used when the malignant cell population is composed primarily of immature lymph cytes or prolymphocytes. We have found th adults, as well as children, with subacute lymph

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cytic leukemia survive significantly longer than those with acute lymphocytic leukemia. It also appears that response to therapy varies for the two subtypes.[8]

Remission Induction

The objective of the initial phase of treatment s complete disappearance of leukemic infiltrates n the bone marrow and extramedullary sites, the estoration of normal hematopoiesis, and the disappearance of all signs and symptoms associated vith leukemic infiltration. When the bone marrow and peripheral blood have returned to normal and there is no clinical evidence of leukemia the patient is said to have obtained a complete remission (Table 1).

TABLE 1

Criteria for Complete Remission In Acute Leukemia

Bone marrow:	**No leukemic cells** **$<$ 5% myeloblasts** **Normocellular** **Normal erythropoiesis, granulopoiesis, megakaryopoiesis**
Blood:	**No leukemic cells** **Hemoglobin $\geqslant$ 11 gm/100 ml** **Granulocytes $>$ 2000/mm^3** **Platelets $>$ 100,000/mm^3**
Symptoms:	**None**
Physical findings:	**Normal**

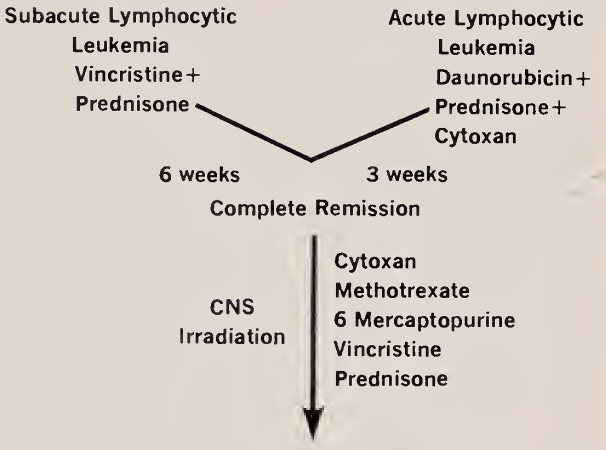
For at least 10 years effective chemotherapeutic egimens have been available for obtaining complete remissions in most children with ALL. In everal large studies prednisone in combination vith either vincristine or 6-mercaptopurine has esulted in complete remissions in more than 80% of children.[9] More myelosuppressive regimens uch as combinations of prednisone, vincristine nd daunorubicin or prednisone, vincristine, 6-mercaptopurine and methotrexate (POMP) ave been reported to give greater than 90% omplete remissions[2] though the numbers of patients studied have been smaller. The combination f vincristine and prednisone is a particularly satisfactory induction regimen because of its limited toxicity.

Until recently, results of chemotherapy in adult ALL have been less encouraging. The above regimens tend to give complete remissions in about 0% of adult patients.[10] In the past few months omplete remissions have been reported in 72% f adults with ALL using vincristine, prednisone nd L-asparaginase[11] and in 78% using a complicated eight drug induction program.[12]

The ideal induction chemotherapy would provide the largest number of patients long term complete remissions using the least toxic drugs. At the Masonic Leukemia Treatment Center we started a protocol for adult ALL in 1971 using different induction regimens depending on the initial morphologic classification. Those patients with subacute lymphocytic leukemia are treated with vincristine and prednisone; those with acute lymphocytic leukemia or acute stem cell leukemia receive daunorubicin, prednisone and cyclophosphamide (Figure). To date 91% (10 of 11) of adult patients have obtained complete remissions.

Treatment of Adult Acute Lymphoblastic Leukemia

(Masonic Leukemia Treatment Center)



Figure

Central Nervous System Prophylaxis

Once effective induction regimens became available, a new problem arose. Patients began developing symptomatic leukemia in the central nervous system (CNS) while their bone marrow and peripheral blood remained free of leukemic infiltration. CNS leukemia rapidly became the most frequent obstacle to prolongation of the initial complete remission. It appeared that antileukemic drugs failed to diffuse into the meninges in effective levels so that residual leukemic cells in that site continued to replicate while their growth was controlled elsewhere. Consequently, treatment regimens to irradicate presymptomatic CNS leukemia involving either craniospinal irradiation or intrathecal chemotherapy or combinations of the two were developed.

While the best method of CNS prophylaxis has not been determined the importance of incorporation of some form of such therapy in ALL treatment programs is clear. In a series of studies of CNS prophylactic therapy in children, Hustu et al. found that 57 of 91 (63%) of children who received no preventive CNS therapy first relapsed with CNS leukemia compared with 11 of 170 (6%) who received high dose irradiation with or without intrathecal methotrexate.[13] Other groups have reported similar results.

The importance of presymptomatic CNS therapy has not been extensively studied in adult ALL, but it is clear that as remission duration is lengthened the occurrence of symptomatic CNS leukemia will become an increasing problem. As indicated in the Figure prophylactic CNS irradiation is part of our current regimen for adult ALL. To date only one patient has first relapsed with CNS leukemia.

Maintenance Chemotherapy

It has been demonstrated in many studies of ALL that if no further chemotherapy is given following induction of complete remission, there is rapid recurrence of the leukemia. Controlled comparisons of patients treated and untreated during remission have documented the advantage of maintenance chemotherapy. It is not clear, however, what constitutes the most effective maintenance regimen. Most include 6-mercaptopurine, methotrexate, cyclophosphamide, prednisone and vincristine as single agents or in various combinations. In children, using these agents, the median duration of hematologic remission has exceeded 52 months.[13]

The duration of complete remission in adults with ALL has not approached that of children. However, a median duration of remission of 24 months has recently been reported.[12] Our current maintenance regimen in adults (Figure) consists of daily oral 6-mercaptopurine, weekly oral methotrexate and cyclophosphamide and monthly courses of vincristine and prednisone. The median duration of remission has not yet been obtained but will be greater than 14 months.

How long maintenance therapy is needed is unknown. Most investigators agree that at some point chemotherapy should be stopped since maintenance chemotherapy carries considerable risk. Maintenance agents are immunosuppressive and as many as 16% of patients die of opportunistic infections during complete remission o their leukemia.[14] Further, long term chemotherapy may result in permanent liver and bon marrow damage, sterility, increased risk of second malignancy, or development of a mor resistant clone of leukemia cells.

The point at which maintenance chemotherapy may be discontinued probably depends o the nature of the previous chemotherapy. Various studies in children suggest that maintenanc chemotherapy may be stopped safely sometim after 12 to 36 months.[3] The St. Jude group has found that about 10% of patients who receive adequate prophylactic CNS therapy an multiple agent chemotherapy for two to thre years relapse following cessation of chemotherapy. This is about the same risk that they fin for dying of infection in remission while o chemotherapy. At present no data are availabl concerning cessation of chemotherapy in adult with ALL.

Reinduction Chemotherapy

In patients with ALL the likelihood of subsequent complete remission decreases with eac relapse and repeated remission induction therap Many patients who relapse on maintenanc chemotherapy can again achieve complete remissions with the same regimen used initially fo induction. More commonly a different, generall more aggressive, regimen is prescribed. Reinduction regimens include L-asparaginase, daunorubicin or cytosine arabinoside combined with various agents. The duration of each successiv remission diminishes. Occasional long term secon remissions occur, especially in children who hav relapsed off maintenance therapy.[15,16] Reinduction chemotherapy for adults with ALL has n been extensively studied.

Survival

It is not possible to state a single survival figure for ALL because it depends on many factor such as age, therapy, and pathologic subtyp The increase in survival of children has bee impressive with some groups reporting a 51 five year leukemia free survival.[3] For adults th survival has not increased as markedly. Gee recently reported a median survival of 45 + month for a group of adult patients.[12] Whether thes improvements in median survival indicate cur remains to be seen.

Acute Granulocytic Leukemia

Diagnosis and Classification

Acute granulocytic leukemia, or acute nonlymphocytic leukemia (ANLL) as it is frequently termed, is a heterogeneous group of diseases characterized by replacement of normal elements by immature cells of the myeloid series. Most adult and a minority of childhood acute leukemias fall into this category.

Four morphologic variants of ANLL based on the preponderant cell type are described: myeloblastic, myelomonocytic, promyelocytic, and erythroleukemia.[17] At the University of Minnesota (Table 2) acute myeloblastic leukemia is further subdivided into two groups—acute myelogenous and subacute myelogenous leukemia.[8] This distinction has been shown to have prognostic significance.

TABLE 2
Classification of Acute Nonlymphocytic Leukemia

	% of Adult cases
Acute myelogenous leukemia	28
Subacute myelogenous leukemia	41
Acute myelomonocytic leukemia	14
Erythroleukemia	14
Acute promyelocytic leukemia	3

The designation of acute myelogenous leukemia is used when the myeloblasts in the bone marrow exceed 60% of the nucleated cell population. The designation subacute myelogenous leukemia is used when the myeloblasts in the bone marrow are less than 60%; substantially more mature myeloid forms are present than in acute myelogenous leukemia. Acute myelomonocytic leukemia is the term used when there is clear differentiation of myeloblasts into both monocytic and granulocytic elements. Generally monocytoid cells and monocytes comprise 20% or more of the leukocyte population in the peripheral blood. Cytochemical demonstration of non-specific esterase in the monocytic cells and elevated serum muramidase levels aid in the diagnosis of this form of leukemia.

The designation erythroleukemia is used for those myeloid leukemias that at diagnosis exhibit striking red cell involvement. The erythroid precursors show morphologic abnormalities such as multinucleation, megaloblastoid nuclei, and cytoplasmic vacuolation. Cytoplasmic periodic acid Schiff positivity of the early red cell precursors is present. A large number of abnormal "promyelocytes" with intense reddish purple granulation indicates acute promyelocytic leukemia. Frequently these cells contain multiple Auer rods.

The distribution of the various subgroups at the University of Minnesota is shown in Table 2. While there is still considerable dispute concerning the clinical usefulness of dividing ANLL into morphologic variants, a number of reports have appeared recently suggesting different treatments and different survivals for the various subgroups.[6,8,18,19]

Remission Induction

Remissions are much more difficult to obtain in ANLL than in ALL. Until recently, complete remissions were rarely achieved in more than 25% of adults. With the development of cytosine arabinoside and daunorubicin relatively effective induction chemotherapy has become available. In the past two years many reports have appeared of greater than 50% complete remissions in adult ANLL using combinations of cytosine arabinoside and daunorubicin, cytosine arabinoside and 6-thioguanine, or cytosine arabinoside, cyclophosphamide, vincristine and prednisone (COAP).[20] Recently a complete remission rate of 87% in adults less than age 60 has been reported using repeated courses of daunorubicin for three days combined with cytosine arabinoside for seven days.[5]

Not only are complete remissions being achieved more frequently, but they are being obtained in patients previously considered refractory to therapy. Patients over the age of 50 were once considered unresponsive to chemotherapy.[21] Several reports[4,22] have recently demonstrated that elderly patients tolerate chemotherapy quite well and may obtain long complete remissions (Table 3). Erythroleukemia was considered a refractory form of ANLL but we[18] have recently obtained complete remissions in 44% of patients using daunorubicin and prednisone (Table 4). Acute promyelocytic leukemia was for-

TABLE 3
Treatment of Patients over 60 with Acute Nonlymphocytic Leukemia (Masonic Leukemia Treatment Center)

	Study 1 1967-71	Study 2 1971-73
Complete remissions (%)	9	42
Median Survival (mos)		
Responders	6.5	15
Non-responders	1	2

TABLE 4
Treatment of Erythroleukemia
(Masonic Leukemia Treatment Center)

	1962-69	1969-73*
Complete remissions (%)	0	44
Survival (mos)		
Median	3	12
Range	1-8	4-26

*All patients treated with daunorubicin and prednisone.

merly one of the most rapidly fatal forms of ANLL because of early death from hemorrhage caused by disseminated intravascular coagulation. Using daunorubicin greater than 50% complete remissions have been obtained.[19]

While more effective chemotherapy for ANLL is now available, induction remains a long and difficult task. At least two cycles of chemotherapy and hospitalizations of four to eight weeks are usually required to obtain a complete remission. Almost all patients with ANLL, in contrast to those with ALL, enter remission only after a period of marked and prolonged marrow hypoplasia. The risk of fatal infection and hemorrhage during the period of marrow hypoplasia is as high as 33% in many studies, and extensive support facilities are required.[20]

Supportive Care

With the availability of platelet transfusions, infection has replaced hemorrhage as the most frequent cause of death during induction chemotherapy. Because overwhelming sepsis may result in rapid death, most leukemia centers empirically initiate broad spectrum antibiotic therapy when the neutropenic patient develops a fever of 101°F.[23] Using high doses of carbenicillin, cephalothin, and gentamicin we have obtained 82% clearance of infection.[24]

Granulocyte transfusions are liberally used in infected patients during periods of marrow hypoplasia. Granulocytes from related donors are obtained using the continuous flow centrifuge or filtration leukapheresis.[25]

The role of protected environments remains controversial. "Laminar flow rooms" and "life islands" seem to decrease the incidence of infection. It has not been proved that they increase survival or the likelihood of obtaining a complete remission.

Maintenance Therapy

Maintenance of complete remission in ANLL remains a difficult problem. Without maintenance chemotherapy, overt leukemia recurs after about two months of remission. Many different combinations of drugs have been utilized in an attempt to extend the period of remission, but most patients on maintenance chemotherapy relapse after six to 12 months. This has been true whether complicated drug regimens involving five to 10 different drugs are used or if the patient simply receives one or two drugs on a weekly schedule.

Some investigators are giving maintenance courses of the original induction regimen at monthly intervals. Other investigators are utilizing immunotherapy alone or in combination with chemotherapy. Immunotherapy most commonly consists of BCG innoculations with or without allogeneic leukemic cells. It is too early to evaluate these approaches but patients who relapse on immunotherapy seem to be easier to reinduce.[20]

Prophylactic CNS irradiation is not used in ANLL. While CNS leukemia has been reported in some patients, patients with ANLL rarely relapse with CNS leukemia while in bone marrow remission. As bone marrow remissions become longer, CNS leukemia may become more of a problem as it has in ALL.

Reinduction Therapy

Reinduction of complete remission in ANLL is much more difficult than in ALL. Occasional long term second complete remissions occur but usually only after prolonged complicated hospitalizations. For those patients who have an HLA-MLC identical sibling, bone marrow transplants have been successful in up to 25% of patients resistant to all chemotherapy.[26] Leukemia has been reported to recur in the donor cells.

Survival

The striking prolongation of survival seen in childhood ALL has not occurred in adult or childhood ANLL. The median survival has slowly but steadily increased. Prior to effective

TABLE 5
Survival in Adult Acute Nonlymphocytic Leukemia
(Masonic Leukemia Treatment Center)

	Study 1 1967-71	Study 2 1971-73
Complete remissions (%)	21	50
Median Survival (mos)		
Responders	14.5	19+
Non-responders	1.5	2
All patients	4.5	10+

chemotherapy, adults with ANLL survived about two months. The median survival for the treatment regimen for adult ANLL that we used from 1967-1971 was 4.5 months (Table 5). The median survival for our present treatment regimen has not been reached but will be greater than 10 months.

It has been clearly documented in ANLL that patients who obtain complete remissions survive longer than those who do not. With the recent development of regimens that yield greater than 50% complete remissions we will probably see increased survival in ANLL. Whether there will be a group of patients with long-term disease free survival remains to be seen.

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Letter to the Editor:

University of Minnesota Medical School

On behalf of the student body and the faculty of the University of Minnesota Medical School, Minneapolis, I wish to express sincere appreciation to the alumni, the Woman's Auxiliary, and physicians and friends of this medical school for the very substantial contributions they have made to the American Medical Association Education and Research Foundation in 1973. The result of the confidence of these many persons has resulted in this school receiving an allocation of $16,339.95. In the United States, eighteen medical schools enjoyed a greater allocation than this amount; eight of these schools were private and ten were state schools. The administration pledges judicious use of these funds in support of the programs of the Medical School. We trust that we can look forward to your continued support in years to come.

N. L. Gault, Jr., M.D.
Dean

Lymphangiosarcoma in

Chronic Post-Mastectomy Lymphedema

J. MICHAEL RYAN, M.D.;* PAUL LOBER, M.D.† and B. J. KENNEDY, M.D.‡

In 1948 Stewart and Treves reported six patients who developed lymphangiosarcoma in the edematous arm after mastectomy.[1] All had developed immediate postoperative edema. Several years later a purplish-red, slightly raised, macular or polypoid lesion appeared on the arm or in the antecubital area; satellite lesions followed and coalesced or remained discrete. The lesions were covered with shiny, atrophic epidermis and frequently became ulcerated. No evidence of metastatic carcinoma was observed in any of these patients who died of pulmonary metastases from lymphangiosarcoma unless surgery cured the disease.

Subsequent reports of this new syndrome were incorporated in a review of 162 patients by Woodward et al. in 1972.[2] Clinically these patients fit the original description of Stewart and Treves although some had only slight lymphedema and others noted increased lymphedema at the time when the lymphangiosarcoma appeared. The mean age of the patients was 68.8 years with a range from 44 to 84 years. There were only two males in the series. The mean duration of lymphedema prior to the appearance of lymphangiosarcoma was 10 years three months with a range of one to 26 years. The site of the initial lymphangiosarcoma was on the upper arm in 75%, the forearm in 18%, the elbow in 4%, and the chest wall in 1%.

Amputation or radiotherapy was the most frequent treatment; some patients were managed by excision, excision and radiotherapy, or chemotherapy alone. The median survival for the group was 19 months. Amputation produced a greater two-year survival rate than radiotherapy ($p < .05$). Analysis of eleven patients who survived more than five years showed that seven had been treated by amputation (four forequarter, three disarticulation); two by wide excision, one by radiotherapy; and one with intra-arterial radioactive yttrium. One patient survived five years after intra-arterial nitrogen mustard. Tumor recurrences usually occurred locally or in the lungs, pleura and chest wall.

A review of the patients seen at the University of Minnesota Hospitals revealed that this disease can occur in the very young woman and also that the pattern of metastatic spread may be unusual.

TABLE
Lymphangiosarcoma in Post-Mastectomy Lymphedema

Case	Age	Duration of Edema To Diagnosis (years)	Survival From Diagnosis (months)	Treatment
1	26	5.2	5	Forequarter amputation
2	69	14	0.75	None
3	72	2.4	16	Radiotherapy
4	54	13	144+	Disarticulation; chest wall recurrence widely resected
5	53	5	21	Wide resection & nitrogen mustard perfusion

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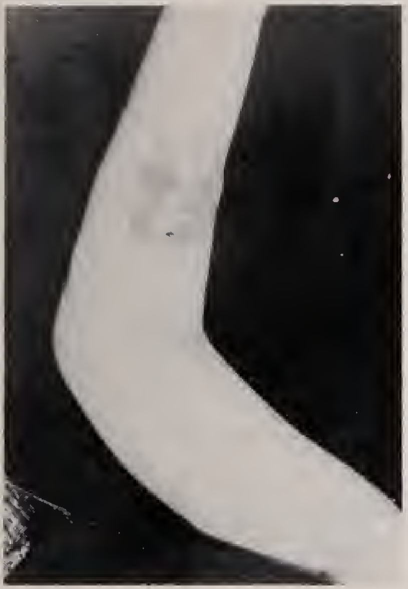

Fig. 1—Gross appearance of the lesions on the arm of Patient #1.

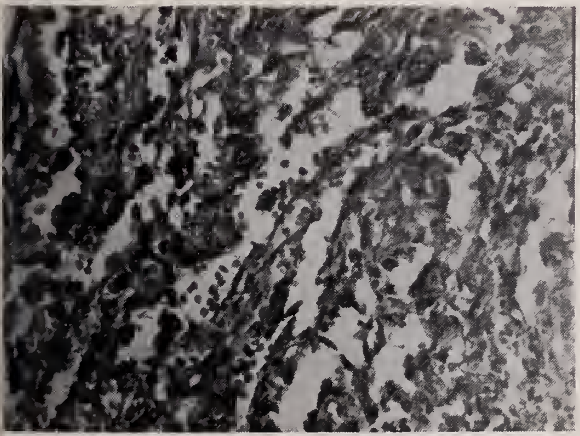

Fig. 2—Sections from the lesions on the arm of Paient #1 show branching channels, lined by plump endohelial cells, infiltrating diffusely. There is cellular irregularity with occasional mitoses. (H and E stain, 250X)

Case Reports

Five patients have been seen at the University of Minnesota hospitals since 1960 (Table). Two patients (#1 and 2) are of particular interest and are described in detail.

Case 1

At the age of 21 years this caucasian woman had a right radial mastectomy with postoperative radiotherapy for a scirrhous carcinoma. A mild lymphedema of the right arm developed postoperatively. An ecchymotic lesion developed on the forearm 4.5 years later. The lesion progressively enlarged over a six-month period with smaller lesions appearing on the upper arm (Figure 1). A biopsy revealed lymphangiosarcoma (Figures 2 and 3). A right forequarter amputation was performed. Three months later she was admitted to the Masonic Memorial Hospital where she died a few days later. Postmortem examination showed widespread lymphangiosarcoma involving the abdominal organs, lungs and myocardium.

Comment

This is the youngest patient recorded with post-mastectomy lymphangiosarcoma; the youngest patient previously reported was 44 years of age.

Case 2

This 69-year-old caucasian woman had undergone right radical mastectomy with postoperative cobalt therapy in 1959. The procedure was followed by chronic lymphedema. Thirteen years later in January 1973 the lymphedema increased and several enlarging nodules appeared on the right arm. A biopsy six months later was considered to be metastatic carcinoma. The patient was unsuccessfully treated with diethylstilbesterol. When she was first seen at the Masonic Memorial Hospital in February 1974 a repeat biopsy showed lymphangiosarcoma (Figures 4 and 5). Review of the initial biopsy also was interpreted as lymphangiosarcoma. Chest Xray, bone scan, and laboratory profile showed no evidence of metastases. Before treatment could be instituted the patient died with the signs of an acute intra-abdominal catastrophe. Postmortem examination revealed extensive intra abdominal hemorrhage and widespread involvement of the mesentery and peritoneum with lymphangiosarcoma; only minimal pulmonary metastatic disease was found.

Comment

The abdominal metastases in this patient presented an unusual pattern. Usually extensive involvement of the chest wall, lungs and pleura is expected.

Discussion

The very existence of the Stewart-Treves syndrome was questioned by Salm in 1963.[3] He reviewed several of the published case reports as well as material from three patients diagnosed as post-mastectomy lymphangiosarcoma at his hospital in Cornwall, England. He contended that the data presented were not sufficient to arrive at a definite diagnosis of lymphangiosarcoma and that the more likely diagnosis in all these cases was metastatic carcinoma. Among published case reports he rejected were the original patients of Stewart and Treves. Salm gave particular emphasis to the importance of reticulin stains which demonstrate the origin of malignant cells within vascular sheaths of reticulin fibers, for diagnosis of vascular malignancies. He emphasized that the material presented by authors reporting rare diseases should leave no doubt regarding the diagnosis and particularly criticized several of the photomicrographs in the literature

One line of evidence suggesting that the Stewart-Treves syndrome did not merely represent misdiagnosis of metastatic carcinoma was the existence of several case reports of lymphangiosarcoma arising in lymphedema in the absence of underlying malignancy. In 1971 Mackenzie reported one patient and collected six other case reports from the literature.[4] All had lymphangiosarcoma by Salm's criteria and the tumors arose in areas of congenital or idiopathic lymphedema. Although he supported an etiologic role for lymphedema in the development of lymphangiosarcoma, Mackenzie agreed that many of the reported cases were not well documented.

Recent advances in this area include the histologic and lymphangiographic studies of Olszewski et al. on experimental post-surgical lymphedema in dogs.[5] Three stages in the development of lymphedema were delineated:

A. Acute edema, in which clinical edema is slight and lymphangiographic changes include dilatation of main lymphatic trunks with appearance of some tortuous collaterals.

B. Latent edema, in which clinical edema is not apparent. During this time there are progressive lymphangiographic changes consisting of dilatation of lymphatic vessels and increasing valve incompetence. Histologic changes likewise show progressive appearance of dilated lymph channels with increased amounts of surrounding connective tissue.

C. Chronic edema, in which clinical edema is marked, and lymphangiographic changes are quantitatively greater than in the latent stage. Electron microscopy shows thickened basement membranes and incompetent interendothelial junctions of lymphatic vessels.

Kitchen described one patient with post-mastectomy lymphangiosarcoma whom he studied with upper extremity lymphangiography.[6] The tumor was promptly outlined by Lipiodol, which re-

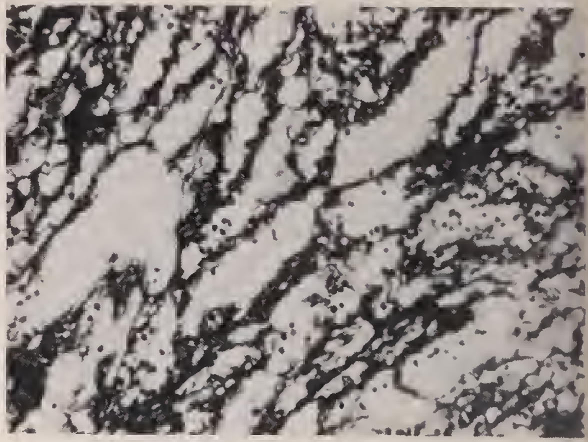

Fig. 3—The same section shown in Figure 2 stained for reticulum. Fibers are shown outlining the channels (Wilder's reticulum stain, 250X)

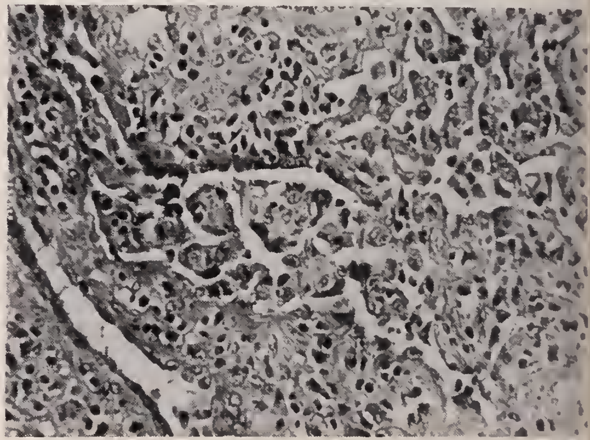

Fig. 4—Sections from a lesion on the arm of Patient #2 show anastomosing channels lined by plump cells. They show relatively large nuclei with prominent nucleoli. There are small numbers of mitoses. (H and E stain, 250X)

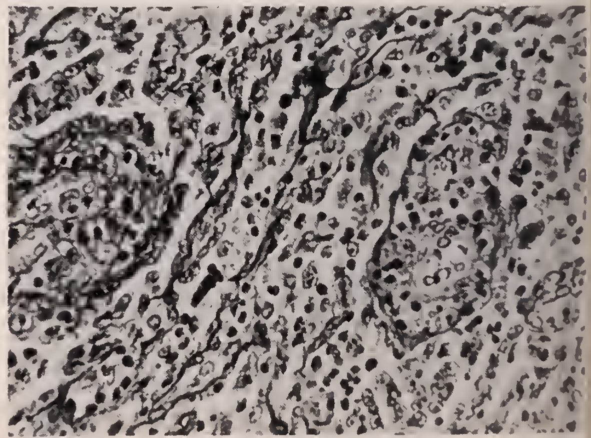

Fig. 5—The same section shown in Figure 4, stained for reticulum. The channels are outlined by fibers. (Wilder's reticulum stain, 250X).

mained within the lesion for at least two days. He proposed that this method might prove useful in determining the extent of lymphangiosarcomas, and the possibility of treatment with radioisotopes injected via the lymphatics.

To detect this disease, a high index of suspicion is necessary on the part of the clinician. Early biopsy specimens treated with reticulin stains may provide prompt diagnosis and an increased number of surgical cures. Certainly frequent biopsy of suspicious lesions will be helpful in establishing the true incidence of the Stewart-Treves syndrome.

Although previous attempts at chemotherapy for this disease have met with only isolated success some newer agents, particularly adriamycin, have shown significant activity against sarcomas and deserve a trial in postmastectomy lymphangiosarcoma.

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Mayo Clinic

Dr. Hillier L. Baker, Jr. has been appointed chairman of the Department of Diagnostic Roentgenology of the Mayo Clinic.

* * * *

Dr. Robert W. Waller has been appointed chairman of the Department of Ophthalmology of the Mayo Clinic.

* * * *

A Fellow in the Mayo Graduate School of Medicine has been awarded first place in the Mead Johnson Excellence of Research Awards presented as part of the Fifteenth National Student Research Forum at the University of Texas Medical Branch, Galveston, Tex.

Dr. Ralph C. Benson, Jr., received the honor for his research, "Immunoreactive Forms of Circulating Parathyroid Hormone in Primary and Ectopic Hyperparathyroidism."

He was one of more than 130 medical students, graduate students in health care sciences, interns, and residents representing 67 medical schools and hospitals who met in Galveston April 24-27 to debate their research at the only meeting of its kind in the United States.

Multiple Myeloma

Clinical Evolution

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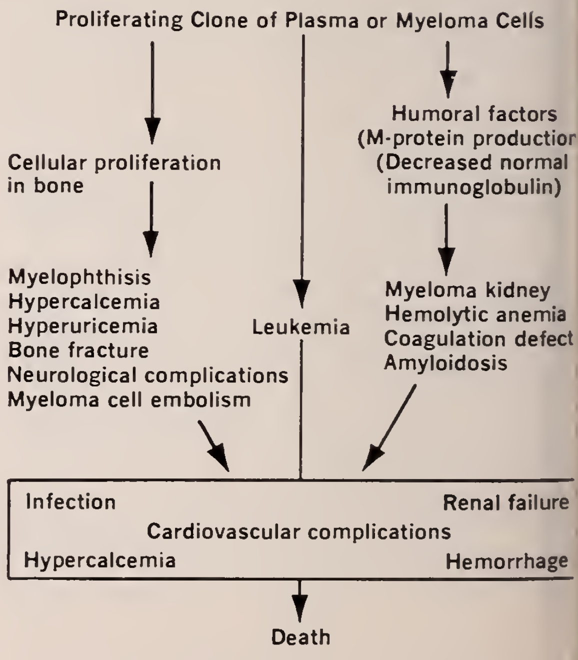
ATHANASIOS THEOLOGIDES, M.D., PH.D.;[‡] ANNE GOLDMAN, PH.D.;[§]
and B. J. KENNEDY, M.D.[£]

This paper reviews the initial symptoms, laboratory findings, and the clinical course of multiple myeloma in 228 patients studied during the past 28 years. There has been no significant change in the age, and sex incidence. There has been no shortening of the duration of symptoms before diagnosis in those patients seen in 1963-71, as compared with those seen in 1943-55. The incidence of initial anemia, azotemia, hypercalcemia, and hypoalbuminemia has not varied significantly through these years. However, an increased occurrence of Bence Jones proteinuria, from 27% in 1943-55, to 54% in 1963-71, was observed. This probably reflects an improvement in laboratory methodology. In this latter period a higher percentage of patients with multiple myeloma had no radiographic osseous lesions.

IN MULTIPLE MYELOMA an uncontrolled proliferating clone of plasma cells results in the production of monoclonal immunoglobulin, bone marrow displacement and bone destruction. These cellular and humoral abnormalities lead to a variety of initial symptoms, serious complications and ultimately death (Figure).

Proliferation of myeloma cells in the bone marrow may result in fractures, neurological complications, hypercalcemia, and myelophthisis. A production of monoclonal paraprotein with a decrease


Proliferating Clone of Plasma or Myeloma Cells
Cellular proliferation in bone
Humoral factors
(M-protein productior
(Decreased normal immunoglobulin)
Myelophthisis
Hypercalcemia
Hyperuricemia
Bone fracture
Neurological complications
Myeloma cell embolism
Leukemia
Myeloma kidney
Hemolytic anemia
Coagulation defect
Amyloidosis
Infection
Renal failure
Cardiovascular complications
Hypercalcemia
Hemorrhage
Death

Figure—Biologic behavior of multiple myeloma.

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See editorial, page 579.

of normal immunoglobulin level may be associated with infections, renal failure, alteration of clotting factors, hemolysis, and amyloidosis. Rarely, the disease evolves into plasma cell leukemia[1] or is complicated by myelomonocytic leukemia.[2,3]

With the greater clinical awareness for multiple myeloma and with the more comprehensive laboratory-patient evaluation, the diagnosis today is probably being established earlier. Since the new nti-tumor therapies and supporting programs are ltering the biologic behavior of multiple myeloma, periodic review of the initial clinical manifesta- ions, the course of the disease and its compli- ations is necessary.

Patients and Methods

The clinical and laboratory findings of 228 atients with multiple myeloma seen at the Uni- ersity of Minnesota Hospitals from 1943 to 1971 vere reviewed. The diagnosis of multiple mye- oma[4] was based on at least two of the following indings: (1) discovery of more than 20% plasma ells in the bone marrow, without other known ause; or presence of less than 20%, but the lasma cells having a neoplastic morphology; or lasmacytoma found in a soft tissue biopsy, (2) resence of Bence Jones proteinuria or monoclonal mmunoglobulinemia, and (3) roentgenographic one lesions. Eight patients with solitary plasma- ytoma or extra-medullary myelomatosis without ither of the other two criteria were excluded.

The study interval from 1943 to 1971 was ivided into three periods: 1943-55, 1956-62 and 963-71. These intervals were selected to provide dequate numbers for comparison.

Results

ge, Sex and Race

The average age at diagnosis of these 228 atients was 61 years, with a range from 31 to 87 ears. Six patients were below 40 and eight above 0. There were 126 males and 102 females. The verage age for males was 61.9 and females 60.4 ll patients but two were white.

There was no significant change through the ree periods in the median age of the patients at e time of diagnosis. The male-female ratio ifted from 2.5:1 in 1943-55 to 1.1:1 in 1956-62 d 0.8:1 in 1963-71.

itial Symptoms

Pain was the chief symptom occurring in 80% of the patients (Table 1). Of these, back pain was present in 50%, extremity pain in 25% and rib pain in 15%. One-fifth of the patients had pain in more than two areas. The next leading symptoms were fatigue and weakness (63%) and weight loss (46%). Neurological symptoms occurred in 20% of the patients as radiculopathy or cord signs secondary to vertebral compression. Lethargy secondary to metabolic abnormalities such as uremia or hypercalcemia occurred in 6.5% of the patients.

TABLE 1
Initial Symptoms in 228 Patients with Multiple Myeloma

Symptoms	Number of Patients Recorded	Incidence of Symptoms %
Pain	226	80
Fatigue and weakness	213	63
Weight loss	194	46
Neurological		
Lethargy	212	6.5
Radicular pain	225	15
Paresthesia	225	5
Paralysis	225	3
Paresis	225	2
Visceral (rectal, bladder)	225	3
Fever	224	9
Infection	224	18
Gastrointestinal	224	14
Bleeding tendency	223	14
Tumor mass	225	8
Asymptomatic	228	4

Nine percent of the patients had fever immediately prior to or during the time of diagnosis; 18% had other signs of infections such as dysuria, cough, cellulitis, or abscess. A bleeding tendency manifested by epistaxis, melena, petechie, hemoptysis or abnormal vaginal bleeding was present in 14% of the patients. Gastrointestinal symptoms consisting of nausea, vomiting, and abdominal cramping pain were reported in 14%.

Tumor was noticed by 8% of the patients. Most of the tumors were due to an expansion of osseous lesions over the ribs and skull. Two patients had soft tissue masses.

There was no difference in the presenting symptoms in the three study periods.

Asymptomatic Patients

The diagnosis of multiple myeloma was established incidentally in nine patients (Table 2). In three patients the diagnosis was confirmed during evaluation of another malignancy, in two during investigation of elevated erythrocyte sedimentation rate, and in one the disease was detected during a family study of myeloma. Three of the nine patients are still alive. One (No. 7) has lived 12 years from the date of diagnosis without any symptoms or treatment; the possibility of plasmacytosis secondary to occult infection or neoplasms has been ruled out both by extensive search and by the twelve year follow-up period. The remaining six patients are dead with a median survival of 2.6 years.

Symptom-Diagnosis Interval

The interval between the onset of symptoms and time of diagnosis varied from day zero for those having an incidental diagnosis of myeloma to eight years, with a median interval of five months. Thirty-eight percent of the patients had an interval of over six months. There was no difference in the duration of symptoms prior to diagnosis in the three periods under comparison.

Laboratory Findings at the Time of Diagnosis

Hemogram: A hemoglobin below 11 gm% was recorded during the initial evaluation in 42% of 203 patients. Of 60 patients evaluated, mild hemolysis was documented in 17 patients. Seven had increased rouleaux formation, and normoblasts were observed in 41 patients. Immature neutrophils were seen in 22% of 187 patients and toxic granules in neutrophils were seen in 49% of 187 patients.

Bone Marrow: Bone marrow preparations were available in 195 patients. The percentage of plasma or myeloma cells varied from 1% to 90%, with diffuse infiltration in nearly one-half of the patients. Large plasma or myeloma cells with nucleoli were noted in the majority of the marrow specimens (147 patients), and mature or small cells with nucleoli in only 32 patients.

Before institution of chemotherapy, there was normoblastic hypoplasia in 57% of 195 patients and megakaryocytes were decreased in 38%. Iron storage was depleted in 10% of 143 patients in whom data had been recorded. However, increased marrow iron was seen in 50% of the patients.

Biochemical Findings: At the time of diagnosis, azotemia as measured by a blood urea nitrogen over 25 mg% was observed in 44% of 180 patients, hypercalcemia in 22% of 157 patients, hyperuricemia over 8 mg% in 47% of 51 patients, and hypoalbuminemia below 3 gm% in 46% of the 191 patients in which the test was done.

A serum monoclonal globulin spike was ob-

TABLE 2
Clinical Courses of Patients with an Incidental Diagnosis of Multiple Myeloma

Case No.	Sex and Age at Diagnosis	Presenting problem	Diagnosis (year)	B. M. plasma cell %	Bone lesion	B. J.	M-protein	Rx (yr)	Status	Survival from Dx (yrs.)	Cause of death
1	F66	Anemia 2° to hemorrhoid	'55	22*	+		r	'58	Dead	6.2	Pneumonia
2	M64	Chronic cholecystitis	'49	2*	+	+		'53	Dead	7.3	Uremia, hypercalcemia
3	F68	Hypertension	'68	9*	+	–	IgG (λ)	—	Alive	3.5+	—
4	F77	Ca. colon 1961, diabetes	'67	16	+		IgG (λ)	—	Dead	2.5	Ca. colon
5	F87	Vaginal bleeding	'62	32*		+	r	—	Dead	0.1	Ca cervix
6	M52	Ca. of tongue	'71	13	+	–	IgA (k)	—	Dead	0.2	Ca. tongue
7	F60	↑ ESR (120 mm)	'59	8*	–	–	IgG	—	Alive	11.8+	—
8	M46	↑ ESR (102 mm)	'62	18*	+	–	r	'63	Dead	2.7	Hyper-calcem hemorrhag
9	F44	Relatives with M-component	'66	19*	–	–	IgA (k)	'69	Alive	5.3+	—

*Presence of immature myeloma cells.
Dx=diagnosis; Rx=treatment; B. J.=Bence Jones proteinuria; r, monoclonal gamma spike.

erved in 132 (71%) of 185 patients. The loca-ion of the spike was over the gamma region in 10, over the beta region in 21 and over the lpha-2 region in one patient. Of 55 patients vith immunoelectrophoresis determinations, 42 ad an increase in IgG and 13 in IgA. The ratio f serum light chain type K:λ was 1.7:1.

Approximately one-third of the patients had nly a serum M-protein, one-third had only Bence ones proteinuria, and one-third had both ab-ormalities (Table 3). Five patients had neither rum M-protein nor Bence Jones proteinuria at ie time of diagnosis. Their diagnosis of multiple iyeloma was reached by marrow study, tumor iopsy or x-ray lesions. One additional patient iitially had a serum M-protein which disappeared fter chemotherapy and remained so even after ie disease had overtly relapsed with more bone ivolvement. The disease was more or less local-ed in two of these six patients. The clinical ianifestations of the remaining four patients osely resembled the non-secretory type of mye-ma.[5] The myeloma cells of these four patients ere morphologically undifferentiated with some resembling reticulum cells.

TABLE 3

Serum M-protein and Bence Jones Proteinuria in 121 patients with Multiple Myeloma

protein	Bence-Jones	Patient number	(%)
+	−	38	(31)
+	+	41	(34)
−	+	37	(31)
−	−	5	(4)
Total		121	(100)

The incidence of anemia, azotemia and hypercalcemia at the time of diagnosis was similar in the three periods. However, Bence-Jones proteinuria was observed more frequently in the period after 1963 (Table 4).

Roentgenographic Studies: Of the 228 patients, 17 did not have Xrays initially. No osseous lesions were evident in 23 patients; generalized osteoporosis as the sole finding was present in 21 patients, and osteoblastic lesions were noted in one patient. Osteolytic lesions were present in 166 patients of whom 71 also had generalized osteoporosis. The majority of patients had osseous lesions in more than two areas. At the time of diagnosis, lesions were limited to the skull in eleven patients, to the spine in sixteen, to the ribs in seven, to the pelvis in three and to the extremities in two. Fractures were observed in 42% of the patients; half of these being manifested as vertebral compression.

When the initial radiographic findings were compared in the patients of the three study periods, it was found that a higher percentage of patients in the 1963-71 period had no osseous lesions and a higher percentage in the 1943-55 period had osteolytic lesions (Table 4).

Complications

The complications of multiple myeloma were evaluated during the course of the disease in 200 patients. Forty-seven percent of the patients had at least one episode of infection. Renal failure developed during the course of the disease in 32%

TABLE 4

Initial Laboratory Findings in Patients with Multiple Myeloma from 1943 to 1971

	1943-55 Pt. No. (%)	1956-62 Pt. No. (%)	1963-71 Pt. No. (%)	P*
Hemoglobin	57	70	76	
⩽11 gm%	34 (60)	35 (50)	42 (55)	NS
Blood urea nitrogen	48	57	75	
⩾25 mg%	25 (52)	22 (39)	33 (44)	NS
Serum calcium	32	55	70	
⩾11.5 mg%	9 (28)	10 (18)	16 (23)	NS
Bence Jones	52	73	76	
positive	14 (27)	34 (47)	41 (54)	<0.01
Serum albumin	48	72	71	
⩽2.9 gm%	24 (50)	33 (46)	31 (44)	NS
Bone marrow	44	62	72	
plasma cell ⩾50%	6 (14)	7 (11)	17 (23)	NS
Skeletal x-ray films	58	71	81	
No lesions	4 (7)	4 (6)	15 (18)	<0.01
Osteoporotic	5 (9)	7 (10)	9 (11)	NS
Osteoporotic & osteolytic	17 (29)	30 (42)	24 (30)	NS
Osteolytic	32 (55)	30 (42)	33 (41)	<0.05

*P=Significance between 1943-55 and 1963-71.

and hypercalcemia in 26.5%. Hemorrhage, including gastrointestinal bleeding, massive epitaxis, hemoptysis and abnormal vaginal bleeding occurred in 16.5%. Neuropathy secondary to cord or root compression was observed in 13.5%. Amyloidosis was found in 4%. Subleukemic plasma cell leukemia with 12% to 30% myeloma cells appearing in the peripheral blood was found in 8 patients (4%).

The type and frequency of the major infectious complications of the 228 patients from 1943 to 1971 were tabulated (Table 5). There has been no apparent change in the type of infection during these years. Bacterial pneumonia and pyelonephritis were consistently the two major kinds of infection. Other miscellaneous infections included cellulitis, abscess, cholecystitis and meningitis.

Opportunistic infections were found in 14 patients; eight patients had herpes zoster, one had lung abscess reflected by pseudomonas EO-1 strain, aspergillosis and candidiasis, one had cytomegalic inclusion disease and mucormycosis, and 2 had moniliasis. Two patients who died of toxoplasmosis have been reported previously.[6,7]

TABLE 5
Type and Frequency of Major Infection in Multiple Myeloma from 1943 to 1971

	1943-55 (62)*	1956-62 (81)*	1963-71 (85)*	Total (228)*
Bacterial pneumonia	19	30	27	75
Pyelonephritis	2	4	9	15
Moniliasis	0	0	2	2
Herpes Zoster	3	3	2	8
Cytomegalic Inclusion Disease	0	0	1	1
Toxoplasmosis	0	1	1	2
Others	8	9	4	21
None	33	40	49	122

*Number of patients.

Associated Neoplasms

In the histories of 228 patients, another primary cancer was noted in 16 patients (7%); adenocarcinoma of colon in four, of prostate in three, of kidney in two, of uterus in two, and carcinoma of adrenal gland, lung, tongue and cervix in one of each. The remaining one patient had four malignant and two benign tumors in addition to the myeloma (seminoma, carcinoma of rectum, basal cell carcinoma of skin, carcinoma of colon, leiomyoma of small intestine and osteoma in skull). Five of his six tumors occurred within a five year interval from the time of diagnosis of multiple myeloma. This patient had a monoclonal IgA of 2,352 mg% in the serum (IgG 880 mg% an IgM 74 mg%), and 20% myeloma cells in th bone marrow. The lymphocyte response to phyt hemoagglutinin stimulation was slightly decrease An electron microscopic examination of a lymp node revealed a normal appearing medulla tissue. Virus particles were not found.

Of these 16 patients, all the tumors but tw occurred before or at the time of the diagnos of multiple myeloma. No incidence of acute my logenous or myelomonocytic leukemia was o served in this series.

Cause of Death

The main cause of death judged clinically w established in 149 patients. Forty-eight patien (32.2%) died of infection. A terminal infectio episode was the cause of death in many patien whose chief complications during the course their disease was neuropathy or uremia. The dea rate secondary to infection was 30% (12/43) i 1943-55, 34% (12/61) in 1956-62, and 31 (14/45) in 1963-71. There appeared to be n change in the incidence of infection as the cau of death in multiple myeloma in recent year even with highly effective antibiotics.

Twenty-nine patients (20% died of uremia, 2 (15.4%) of cardiovascular diseases, nine (6% of hypercalcemia and eight (5.4%) of hemo rhage. The number of patients in the three perio dying from these complications is too small f meaningful comparison. In only one patient w the cause of death due to drug toxicity. Th patient developed staphylococcal sepsis with white blood cell count of 900 as a result chlorambucil therapy.

In the remaining 23 patients (15.4%), t cause of death was apparently due to the disea process with severe cachexia but without eviden of the complications referred to above.

Postmortem Findings

Postmortem examinations were performed 60 patients (Table 6). Pneumonia was the mo frequent finding occurring in one-half of t examinations. Of special note was the presence myeloma kidney in 14 patients (23%). Am loidosis was demonstrated in seven patients. Ge eralized amyloidosis was seen in five patients a local amyloid changes were seen in two patien one in the basal membrane of the glomeruli a he other in the media of pulmonary vessels. One dditional patient had amyloidosis established by ectal biopsy; an autopsy was not performed on his patient. Seven of the eight patients with myloidosis were female. Bence Jones proteinuria vas positive in five of the seven patients with myloidosis who had urine protein electrophoresis erformed.

Two patients had extensive myelofibrosis; one ad osteosclerotic lesions and subleukemic plasocytic leukemia and the other had severe thromocytopenia. Pulmonary emboli occurred in seven f 60 patients. Four were due to marrow myeloma mboli and one was due to myeloma cell emboli ut without the presence of any normal marrow ells.

Comment

The analysis of the clinical and laboratory data om 228 patients with multiple myeloma observed ver a 28 year period provides a general view of e natural history of this disease and an evaluaon of changes in the biological and clinical beavior through these years. The application of ore sophisticated technology such as protein ectrophoresis and immunoelectrophoresis was ost probably responsible for the increased rate positivity of Bence Jones proteinuria from 1943 1971. Patients without visible bone lesions or iagnosed incidentally were more often seen rentl y because of the routine use of the protein ectrophoresis. However, in general, based on e results of the median age at the time of diagnosis and the duration of symptoms before diagnosis, there is no indication of an earlier diagnosis of symptomatic multiple myeloma in 1963-71 than in the 1943-55 period.

Infection has been the chief complication and main cause of death. The type and incidence of infection have not changed in the past 28 years in this study. It has been reported that Gram negative bacterial infection has become the predominant type of infection in multiple myeloma in the recent three years.[9] The incidence of other complications in this study, such as renal failure, hypercalcemia, hemorrhage and neuropathy, was comparable to other reported series.[10,11]

In the postmortem examination, of the seven patients with pulmonary emboli, five were due to myeloma cell emboli. Tumor embolism is a well known phenomenon; however, tumor emboli caused by myeloma cells has been emphasized infrequently.[12]

Husselmann reported that deposits of primary amyloid may occur in normal individuals over 70 years of age.[13] All of the patients complicated with amyloidosis in this study were below 70 years old. Osserman et al. stated that Bence Jones proteinuria was found virtually in all their patients with primary amyloidosis.[14] Snapper and Kahn further implied that paramyloidosis as a rule did not develop in myelomatosis in the absence of Bence Jones proteinuria.[15] This concept is supported by the recent finding that amyloid fibril proteins are derived from homogeneous immunoglobulin light chains.[16] In this study, Bence Jones proteinuria

TABLE 6
Autopsy Findings in 60 Patients with Multiple Myeloma

Lungs:		Metabolic:	
Bronchopneumonia	29	Paramyloidosis	7
Pulmonary emboli	7	Metastatic calcification	5
(myeloma emboli)	5	2° parathyroid hypertrophy	2
Hydrothorax	7	Myeloid metaplasia	6
Heart:		Myelofibrosis	2
Myocardial infarction	8	CNS:	
Marantic or mural thrombi	2	Myelo-encephalomalacia	5
Myocardial fibrosis	2	Meningitis	2
GI:		Infection:	
Liver cirrhosis and fatty infiltration	5	Septicemia	6
Cholecystitis and/or cholelithiasis	6	Toxoplasmosis	2
Pancreatitis	4	Mucomycosis	1
Gastric or duodenal ulcer	5	Cytomegalic inclusion disease	1
Colitis	5	Tumor:	
Renal:		Thyroid adenoma	8
Myeloma kidney	14	Adrenal adenoma	2
Vein thrombosis	2	Islet cell adenoma	2
Pyelonephritis	7	Harmatoma (lung)	1
Calculi	2	Hemangioma (liver)	1
		Renal carcinoma	1
		Prostate carcinoma	1
		Squamous cell carcinoma	1

was positive by electrophoretic method in five of seven patients with myeloma and amyloidosis.

The issue of increased incidence of neoplasm in patients with multiple myeloma has attracted attention since Weitzel analyzed the autopsy results of 57 patients with myeloma and found cancer in 11 cases, an incidence of 20%.[17] However, Snapper and Kahn reported that additional cancer was found in only two of 91 autopsies.[15] Berg, in a prospective study of the incidence of multiple primary cancers, found 13 patients with a second cancer in 207 multiple myeloma patients.[18] In our retrospective study 16 patients had a second cancer during their lifetime, an incidence no greater than that of Berg who did not believe that there is a significant increased risk of a second cancer for myeloma patients.

Although a few plasma cells may frequently be found in the peripheral blood, plasma cell leukemia is rare. There has been a number of myeloma patients with an increase of plasma or myeloma cells in the blood with normal white blood cell count. This pattern could be referred to as subleukemic plasmacytic leukemia. With this definition, eight patients had subleukemic plasm cell leukemia. This group of patients had a uniformly poor prognosis with a median surviv of only 92 days (ranging from 15 to 383 days from the date of diagnosis.

According to the clinical manifestation and th extent of the disease involved, multiple myelom has been classified into four stages; early incipie or asymptomatic, symptomatic, advanced an fulminant leukemia.[19] The clinical course is d termined by the stage and the degree of compl cations. In a slowly proliferating type of myelom the patient may remain asymptomatic for man years. The indication for treatment in this grou of patients is a controversial issue; many recon mending observation without treatment. Onc symptoms emerge, the disease can perpetuate itse into an irreversible patho-physiological proce with various complications. Chemotherapy at th stage frequently can reverse the trend and rend its maximal benefit. However, once the diseas evolves into an advanced stage of leukemic phas treatment is usually less effective in prolongin survival.

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Southern Minnesota Medical Association's
Annual Meeting

This year the Association will meet September 21 in Judd Hall in Rochester. The program will be printed in the August issue.

Malignant Bone Tumors in Children

Recent Advances in the Treatment

PETER F. COCCIA, M.D.*; WILLIAM KRIVIT, M.D., Ph.D.;† and MARK E. NESBIT, JR., M.D.†

This article outlines the major obstacles which have prevented any significant uccess in the treatment of malignant bone tumors, discusses the diagnostic evaluation of a patient with a suspected malignant bone tumor, and presents information on recent changes in the treatment of osteogenic sarcoma and Ewing's sarcoma.

THE TREATMENT OF malignant bone tumors in hildren and young adults has been discouraging. ures have been possible in less than 20% of ases, even for patients with apparent clinically ocalized disease. Bone cancer is fortunately rare n children, accounting for only 3.4% of all childood malignancies.[1] The two most common maignant lesions in children are osteogenic sarcoma nd Ewing's sarcoma.

bstacles to Control of Malignant Bone Tumors

Many advances have been made in the treatment of cancer in children during the past 10 ears. Survival is improved for Wilms' tumor, cute lymphoblastic leukemia, and rhabdomyoarcoma. Certain obstacles have prevented a simiar improvement in the treatment of bone tumors.

An initial obstacle is the inability to make an arly diagnosis. Bone pain is the only consistent ymptom. It is a vague complaint that usually oes not make parents or physicians think of omething as serious as cancer. They most often ink of trauma, "growing pains," rheumatic fever, r infection. The average patient with osteogenic arcoma is first seen by a physician after three onths of symptoms, the average patient with wing's sarcoma after six months. Systemic sympms other than pain are uncommon. Occasionly patients with Ewing's sarcoma present with iking fever and have an associated leukocytosis, anemia, and an elevated sedimentation rate that suggests synovitis or osteomyelitis. The early development of widespread metastases is obviously due to unrecognized but viable tumor deposits present at the time of initial diagnosis. In osteogenic sarcoma, these metastatic lesions occur almost exclusively in the lungs but bone metastases should not be overlooked.[2] In Ewing's sarcoma, the metastatic deposits are usually not confined to the lungs but can include bones and bone marrow, lymph nodes, liver, and central nervous system.[3]

A second major obstacle to the effective diagnosis of bone tumors is the lack of any collaborative laboratory studies. Most blood studies are not useful. Serum alkaline phosphatase is often elevated in osteogenic sarcoma but it is elevated in numerous other conditions where osteoid is produced. The erythrocyte sedimentation rate can also be elevated, especially with Ewing's sarcoma.

The greatest obstacle has been the lack of consistently effective treatment for primary and metastatic lesions. To completely eradicate the primary lesion with radiotherapy, doses above 5,000 rads (Co^{60}) are necessary. For osteosarcoma even doses of 7,000-9,000 rads are not enough to ensure complete response. Effective chemotherapy has been completely lacking for osteogenic sarcoma, though several chemotherapeutic agents have been successful in producing partial regression in metastatic Ewing's sarcoma.

Diagnostic Evaluation

Differential Diagnosis

In the initial differential diagnosis of a bone

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lesion, both benign and malignant conditions must be considered. Fortunately most such lesions in infants and children are benign cysts and cartilaginous tumors.[4,5] Less common are the nonneoplastic disorders which cause bone destruction and mimic bone tumors. Examples are eosinophilic granuloma,[6] osteomyelitis and myositis ossificans.[7] Rare but of more serious consequence are the primary and metastatic lesions which involve bone.

Evaluation of the Patient

Extensive diagnostic procedures are necessary to establish the diagnosis and delineate the extent of disease in a suspected malignancy of bone. The first step is adequate roentgenographic examination. Both antero-posterior and lateral projections of high technical quality of the whole suspected lesion should be obtained. Films of the opposite extremity are sometimes helpful. It is important to find the extent of the lesion and to determine which area would be most representative to biopsy. Separate films for bone and soft tissues and supplemental views in other positions may be helpful. Tomography is useful when multiple bony structures are superimposed, bony sclerosis has occurred, areas of soft tissue calcification are detected, or a fracture is present. Xeroradiography and angiography offer detailed visualization of bone and adjacent soft tissue. Isotopic scans probably are of little additional value in studying a primary lesion but are important in detection of metastatic lesions. An excellent monograph[8] is available discussing the roentgenographic diagnosis of malignant bone tumors.

An adequate representative open biopsy under general anesthesia is necessary to diagnose a bony malignancy. A diagnosis and definitive treatment based solely on examination of frozen section material is not recommended. Frozen sections are valuable to determine if adequate sampling has been done. Because many lesions are quite necrotic or have uninvolved reactive inflammatory tissue surrounding them, deep biopsies containing material from both bone and soft tissue should be obtained.

The histology of various bone tumors may be similar and pathologists may have difficulty differentiating various tumor types. Osteogenic sarcoma has frequently been confused with myositis ossificans[7] and infantile cortical hyperostosis (Caffey's disease).[9] Even more difficult is the differentiation of the small round cell tumors of which Ewing's sarcoma is an example. The lesion is confused histologically with other malignancies such as reticulum cell sarcoma,[10] metastatic neuroblastoma, and metastatic retinoblastoma and with benign lesions such as eosinophilic granuloma and osteomyelitis. Sophisticated tests such as electron microscopy or tissue culture evaluation may be useful.

It is important to stage the patient for possible metastatic disease. Staging is valuable for detecting subclinical metastatic disease, preventing unnecessary amputations, influencing therapy and giving some prognostic indication. It serves as a baseline for followup studies after definitive therapy has been completed.

Pulmonary radiography with antero-posterior, lateral and both oblique views and full chest tomograms should be performed to search for pulmonary metastases. Skeletal surveys, bilateral trephine bone marrow biopsies and aspirates and isotope scanning should be performed to determine whether the skeleton as well as marrow cavity is free of metastatic disease.

Early metastatic lesions in the skeleton may go undetected by radiographic examination because a 30-50% change in medulary cavity bone density is required to produce visible changes on x-ray film. Isotopic scans are capable of detecting very small metastatic lesions in bone and sometimes even pulmonary metastases. Bone scanning has been cumbersome using isotopes with long half-lifes (^{47}Ca, ^{85}Sr) which deposited in bone and carried risk of radiation damage. They were seldom employed in children. With the advent of total body scanning devices that produce a "minified" image and the employment of isotopes with a short physical half-life (^{99m}Tc polyphosphate, ^{18}F, ^{87m}Sr, ^{75}Se methionine, and ^{67}Ga) isotopic scans have become more useful. Scanning time is short and radiation dosage low so these methods can be used in children with little danger and a minimum of discomfort. The new isotopes and detectors often provide excellent resolution and suggestive evidence of metastatic disease when conventional roentgenograms are nondiagnostic. Suspicious areas should be biopsied.

Treatment

The treatment of malignant bone tumors in children is often difficult due to late diagnosis, doubt as to morphological classification, and early metastases. Recent advances in treatment of both osteogenic sarcoma and Ewing's sarcoma have resulted in more successful treatment of the primary lesion, subclinical metastases, and metastatic disease.

Osteogenic Sarcoma

Though patients with osteogenic sarcoma often present with only a localized tumor, 80-90% of these patients develop multiple pulmonary metastases within six to nine months. These lesions rapidly coalese and produce bulky solid tumor filling the pulmonary cavity and frequently lead to pneumothoraces. Metastatic lesions have rarely responded to radiotherapy alone or standard chemotherapeutic agents. Most centers recommend immediate amputation for accessible primary lesions and no evidence of distanct metastases.[11] Cade[12] recommended high dose radiotherapy (6,000-10,000 rads at 1,000 rads/week) followed by radical ablation three to six months after radiotherapy f pulmonary metastases do not develop. Experience at several centers has shown a lack of uniform ocal control with high dose radiotherapy.[13] The present recommendation for accessible primary esions is surgical. In patients with inaccessible primary lesions and metastases present at diagnosis, radiation therapy is the initial treatment of choice.

For those with metastatic disease, various chemotherapeutic agents[14] such as cyclophosphamide, vincristine sulfate, actinomycin D, mitomycin C and phenylalanine mustard have occasionally produced a temporary regression but no cures. The only patients with metastatic disease that have shown long-term survival have been a select group of patients who have had surgical resection of pulmonary metastases.[15] Most of these cases represent patients who develop a small number of metastases one year or more following the initial diagnosis. It now appears that effective chemotherapeutic programs have become available. Impressive results with adriamycin and high dose methotrexate with citrovorum rescue or a combination program using these drugs have been recently reported (Table 1).

Following the successful programs used in the treatment of Wilms' tumor and rhabdomyosarcoma where effective chemotherapeutic agents were used in conjunction with primary therapy, several medical centers have been piloting treatment programs using chemotherapy in combination with curative treatment to the primary (Table 2). This table showing 42 of 59 reported patients with localized osteogenic sarcoma are free of disease one to 18 months, is a significant improvement over previous statistics.

Ewing's Sarcoma

The primary lesion in Ewing's sarcoma is cur-

TABLE 1
Recent Advances in the Treatment of Metastatic Osteogenic Sarcoma

Series	No. of Patients	Treatment Program	Results
Jaffe, et al.[16]	10	High dose methotrexate plus citrovorum rescue alone or in combination with radiotherapy	Regression in 4 of 10
Cortes, et al.[17]	17	Adriamycin	Regression in 7 of 17
Gottlieb, et al.[18]	18	Adriamycin + DTIC	Partial regression in 8 of 18 patients
Rosen, et al.[19]	11	Vincristine sulfate, high dose methotrexate plus citrovorum rescue, adriamycin and cyclophosphamide	4 had partial response lasting 5 months to 12+ months
Wilber, et al.[20]	8	High dose methotrexate plus citrovorum rescue, vincristine sulfate, adriamycin, cyclophosphamide plus radiotherapy	8 of 8 had some response, 3 with >50% regression
Nesbit[9]	4	Mitomycin C, pulmonary radiation plus surgical resection of metastatic disease	2 of 4 alive over 5 years

TABLE 2
Recent Advances in the Treatment of Localized Osteogenic Sarcoma

Series	No. of Patients	Treatment Program Following Amputation	Results
Pratt, et al.[21]	5	adriamycin, cyclophosphamide and high dose methotrexate plus citrovorum rescue	5 of 5 patients disease free for 4, 4, 7, 9, & 11 months
Cortes, et al.[17]	20	adriamycin—courses given every 28 days for six courses	15 of 20 patients free of disease 1+ to 23+ months (median 5.5 mos.)
Wilber, et al.[20]	5	vincristine sulfate, adriamycin, cyclophosphamide, high dose methotrexate plus citrovorum rescue	4 of 5 patients disease free 12+, 12+, 10+ and 7+ months
Sutow[22]	18	vincristine sulfate, cyclophosphamide, L-sarcolysin and adriamycin over a 72 week period	10 of 18 (55%) remain free of disease 15 months or longer from time of amputation
Jaffe, et al.[23]	11	High dose methotrexate plus citrovorum rescue every 3 weeks for 2 years	10 of 11 disease free for 1+ to 18+ months (median 8)

able in a high percentage of cases with radiotherapy. Amputation is rarely indicated. Radiation doses to the primary lesion between 4,000 and 7,000 rads are recommended, Supervoltage or Co^{60} sources should be employed and the entire bone and surrounding tissue treated. Additional treatment to the local lesion is usually recommended. Despite the high frequency of local control, cure is seldom effected because of hematogenous dissemination to lungs, bones and lymph nodes. Only 10% of patients treated with local therapy are cured. Undetected metastases are usually present at the time of diagnosis and patients with apparently localized tumor must be treated with systemic therapy.[24]

In contrast to osteogenic sarcoma, there have been effective chemotherapeutic agents available for the treatment of metastatic disease. Vincristine sulfate,[25] cyclophosphamide,[26] 5-fluorouracil,[27] actinomycin D,[28] adriamycin,[29] BCNU[30] and DTIC[18] have all shown clinical usefulness. Most investigators[24,31,32] now employ combinations of two to four of these agents in intensive regimens as adjunctive treatment to localized disease as well as for treatment of documented metastatic disease. The use of prophylactic bilateral pulmonary irradiation (1,200-2,000 rads)[24] and even total body irradiation[33] has also been advocated because of the high incidence of pulmonary metastases and the fact that small metastatic deposits are curable with radiotherapy. Prophylactic CNS irradiation has been suggested[34].

A multi-institutional study, the Intergroup Ewing's Sarcoma Study, was begun in July, 1973 to access the benefit of these various treatment modalities. It is hoped that such a study will be able to access the value of each therapy and therefore determine the best therapy which is associated with the least morbidity.

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15-34. Will be found on page 561.

Management of Pheochromocytoma

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In caring for these patients and reviewing their clinical records a number of points evolved which are not emphasized in standard sources: (1) With a suspected pheochromocytoma, arteriography, if it is to be carried out, should be done only after alpha adrenergic blockade. A physician familiar with the use of blocking agents and norepinephrine should be present with the patient during the procedure. (2) Arteriography can prove helpful but is not essential unless the flank approach is to be used to remove the lesion. (3) Inability to visualize a tumor in one site does not relieve the surgeon of the obligation to search all other areas containing chromaffin tissue. (4)Wide fluctuations in blood pressure and need for large volumes of transfused blood are minimized by adequate preoperative preparation with Phenoxybenzamine. (5) The correct dose of Phenoxybenzamine is the amount required to correct hypertension. In practice, this is frequently as much as 200 mgm per 24 hours. (6) The operative approach may be either transabdominal-transperitoneal or flank-retroperitoneal, depending upon the probability of multiple lesions, the certainty of arteriographic localization, the size of the identified lesion, the cardiopulmonary status of the patient and his habitus. (7) Palpation alone, without opening the retroperitoneal space, is inadequate to rule out an adrenal pheochromocytoma. (8) Multiple lesions may occur within one gland.

THE FASCINATING PROBLEM of pheochromocytoma has been amply reviewed in numerous journal articles and textbooks.[1-3] The purpose of this paper is not to discuss the whole subject but rather to relate some instructive experiences and some pitfalls to be avoided. Certain of the points to be made are found in standard works but are not adequately emphasized; others may be contrary to generally accepted dogma.

Localization of the Lesion

Establishing the presence of a pheochromocytoma depends on biochemical abnormalities, specifically, elevated serum catecholamines and excessive urinary excretion of the metabolites, Vanilmandelic acid (VMA) and metanephrine.[4] Establishing the exact location of the tumor depends on radiologic studies. Differences of opinion prevail regarding the need for and the accuracy of radiologic localization and regarding the hazards of arteriographic procedures in this setting.

Nine of our patients were subjected to intravenous pyelography, most with tomograms; in only two instances did the study forecast the site of the tumor. The location of the pheochromocytoma was correctly identified in seven of ten preoperative arteriograms. The three angiographic failures were as follows: One, a right suprarenal tumor, 3.5 by 4 cm in diameter, was not seen on either angiogram or selective renal arteriogram. Two, a 4 by 5 cm right suprarenal pheochromocytoma was correctly identified but a 2 cm lesion in the left adrenal gland was not appreciated. Three, a 10 by 5 cm pheochromocytoma was visualized in the left suprarenal position but a 3 by 2.5 cm lesion in the right adrenal was not seen on the arteriogram. In the last case, repeat study after operation did show the right sided lesion.

An important localization by angiograms was accomplished as follows: Preoperative roentgen studies were not done. A 5 by 4 cm lesion was removed from the right suprarenal area and on careful exploration no other lesions were found. An aortogram, done after hypertension failed to subside postoperatively, revealed a three cm tumor blush to the left of the aorta four cm below the origin of the renal artery. Preoperative angiography in this instance would almost certainly have demonstrated the lesion and avoided the need for reoperation.

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See editorial, page 579.

If the pheochromocytoma can't be palpated in the neck or seen in the mediastinum on chest Xray, it will almost certainly be found in the abdomen. Whether an adrenal pheochromocytoma lies on the right or left is of little moment if the surgeon chooses the abdominal approach and exposes both glands directly. If, however, a flank approach is to be used, preoperative localization is essential. Aortography may also identify extra-adrenal or multiple tumors and provide important information on the anatomy of the renal arteries.

Failure to identify a pheochromocytoma by arteriography is a fairly frequent occurrence. Negative roentgen findings do not absolve the surgeon from searching all areas where lesions might be found. One can argue, therefore, that there is no place for this procedure. We have concluded that arteriography is not an essential part of the preoperative workup. It proves quite useful in certain instances, and these are unpredictable. Intravenous pyelography with tomograms should be done with the possibility of localizing the tumor but more to establish the integrity of bilateral renal function.

Potential Hazards of Angiographic Studies

Case Report

A 13-year-old female was hospitalized with chief complaints of blurred vision and spots in front of her eyes. Admission history recorded the additional symptoms of severe headaches for three months prior to entering the hospital, episodic pallor, weakness, palpitations, and heat intolerance. On physical examination the patient was found to be hypertensive. Pheochromocytoma was included in the diagnostic possibilities and urine was collected for measurement of catecholamine metabolites. The house office, in the hope of expediting the diagnostic workup, arranged for aortography, which did show a right suprarenal tumor. Shortly after injection of the contrast medium, the girl developed agitation and disorientation which progressed to grand mal seizures and coma. Endotracheal intubation and ventilatory assistance were required. Arterial blood pressure was recorded as 180/100 associated with tachycardia. The attending physicians recognized the situation and administered intravenous Regitine and Propranolol with partial correction of hypertension and tachycardia. After returning to the ward, the patient's skin was noted to be extremely warm and the rectal temperature proved to be 108°F. Ice packs were applied and intravenous Phenoxybenzamine administered. Two days passed before the girl had recovered sufficiently to take oral sustenance.

For seven of the other arteriographic studies, the patient had been prepared in advance with alpha adrenergic blockade and no complications attended the procedure. An additional two patients, in whom the diagnosis was not appreciated, were subjected to arteriograms in the absence of blocking agents but no problems developed.

When pheochromocytoma is suspected, an arteriographic "fishing expedition" is extremely hazardous. Before such studies are pursued, the patient should be given sufficient alpha adrenergic blocking drug, Phenoxybenzamine, to bring the blood pressure to near normal. The beta adrenergic blocker, Propranolol, should also be administered to avert arrythmias. Alternatively, an intravenous infusion can be started before injection of the contrast material to administer Phentolamine and Propranolol, as needed, to counter hypertensive episodes or arrythmia. This seems a less satisfactory means of dealing with the problem. In any event, a physician who understands possible complications and the use of the various pharmacologic agents should be present. The arteriographer must, of necessity, attend to the diagnostic study and should not be responsible for drug administration.

Pharmacologic Preparation for Operation

Case Reports

This case was the subject of a previous report.[5] A 32-year-old woman had a four year history of episodic headaches, palpitation, anxiety, tremor, and blurred vision. The frequency of these spells had recently increased. Five weeks before entering the University Hospitals, she was found by her private physician to have elevated VMA and catecholamine excretions. Repeat urine samples were collected. Three weeks later, while awaiting results, the patient experienced an episode of syncope. At a community hospital she was found to have an arterial blood pressure of 240/130 and was treated with Phentolamine. Two hours later the blood pressure was said to be unobtainable. At this time the patient complained of severe right flank and abdominal pain. Intravenous norepinephrine was required to restore and sustain the blood pressure for the next 24 hours. At the time of transfer to the University Hospitals, physical examination showed marked right sided abdominal tenderness. Chest Xray and auscultation both gave evidence of pulmonary edema. The circulation stabilized during the next two days with vigorous pharmacologic support. In the subsequent two weeks, arterial blood pressure was perfectly normal and urinary norepinephrine excretion was within normal limits. The explanation for this sequence of events became apparent at operation. A 60 gm pheochromocytoma removed from the right suprarenal region was found to be largely hemorrhagic and necrotic. In effect, the tumor had already been removed by necrosis. The lesson is that once the diagnosis is firmly established, drug treatment should be instituted promptly and operation carried out without undue delay.

Occasionally, early operation is not feasible and drug management is prolonged.

A 16-year-old girl entered the hospital with retinal angiomas, headaches, hypertension, and papilledema. Angiograms revealed a cerebellar hemangioblastoma and Von Hippel-Lindau syndrome was diagnosed.[6] During the course of an operation to remove the cerebellar lesion, the patient developed severe hypertension with systolic pressures above the level measurable with a mercury manometer and then had a nearly fatal episode of pulmonary edema. She eventually recovered from the effects of the operation and the hypertensive crisis, although for two weeks she was severely obtunded and required respiratory support. The patient was not discharged for two months, at which time she still had a substantial cerebral deficit, mild intellectual impairment, motor weakness, and incoordination. Oral Phenoxybenzamine, in doses of 75 mgm every twelve hours, plus Propranolol, 20 mgm four times a day, maintained perfect control of blood pressure and complete freedom from symptoms for just over a year, at which time bilateral adrenal pheochromocytomas were removed.

The lesson from this and other experiences is that the effects of catecholamine excess can be controlled for prolonged time periods with adequate doses of adrenergic blocking agents.

This 16-year-old girl, with Von Hippel-Lindau syndrome. provided another important, although inconclusive, observation.

As noted above, we removed bilateral suprarenal pheochromocytomas. Although an attempt was made to preserve some of the adrenal cortex, little viable tissue remained after a 37 gm pheochromocytoma was removed from the right side. The left adrenal lesion weighed 7 gm and was distinctly encapsulated, grossly and histologically. It was possible to preserve most of the apparently normal left adrenal cortex with its blood supply intact. The patient subsequently was supported with steroids but eventually tolerated their withdrawal. An ACTH stimulation test demonstrated adequate adrenal cortical function. Two months following this operation, she required enucleation of an eye because of retinal detachment and painful glaucoma. During the procedure there was again elevation of blood pressure and tachycardia. Urine VMA and metanephrines collected during this hospitalization proved to be within normal limits. The patient was then free of symptoms for another six months when she began to experience sweating episodes. A year after the removal of the bilateral pheochromocytomas, hypertension recurred. At this time urine metanephrines were slightly elevated. Repeat angiographic study demonstrated another pheochromocytoma in the left suprarenal area. After Dibenzyline blockade, a three cm round tumor was removed.

One lesson from this case is that pheochromocytomas, particularly when associated with syndromes, may not only be bilateral but may be multiple within each adrenal gland. The second point is that a pheochromocytoma can grow quite rapidly. A residual tumor, which could not be palpated at the original operation, was fully three cm in diameter just a year later. This is not to say that in removing bilateral pheochromocytomas attempts to preserve adrenal cortical function are inappropriate. One must weigh the possibility of an undetectable residual pheochromocytoma versus the hazards of a lifetime of adrenal cortical insufficiency and steroid administration.

With regard to preoperative preparation, four of nine patients so treated required 200 mgm of oral Phenoxybenzamine per day to bring blood pressure into normal ranges. The standard dose is one mgm per kg per day but the correct dose of this agent is the amount required to obtain freedom from symptoms and hypertension. This point is not universally appreciated and should be emphasized.

Oral Phenoxybenzamine should be started at least five days before operation. The older literature repeatedly emphasized that patients with pheochromocytomas have functionally contracted blood volume and that excision of the tumor with consequent release from excess catecholamine effects may be followed by profound hypotension, which will respond only to norepinephrine infusion. It was subsequently realized that the hypotension following tumor removal could be markedly ameliorated by transfusing quantities of blood equal to approximately twice the measured operative loss. Release from chronic vasoconstriction apparently leads to excessive vasodilation and an acutely expanded intravascular space.

Nine of our operations were preceded by adequate Dibenzyline preparation. In none of these instances was norepinephrine support of arterial blood pressure required after removal of the tumor. Blood replacement approximately equaled the measured blood loss in each. In only one patient did the systolic blood pressure exceed 180 mm of Hg at any time during the operation. This man was subsequently found to have renovascular hypertension in addition to pheochromocytoma.

To be contrasted are four patients who received only intraoperative alpha adrenergic blockade with Phentolamine. The maximum intraoperative systolic blood pressure exceeded 240 mm of Hg in each instance. Required blood replacement was twice the measured loss in three of the four procedures. Norepinephrine infusion was needed to sustain arterial pressure following removal of the tumor in two of these four operations.

The chronically effective alpha adrenergic blocking agent, Phenoxybenzamine, has been available only in recent years. Numerous pheochromocytomas were successfully removed without the help of adrenergic blocking agents but with reported mortality rates as high as 25%.[7] Under the circumstances of sustained hypertension and attendant atherosclerosis, one is well advised to minimize intraoperative fluctuations in blood pressure. Tachycardia and rhythm disturbances are largely dependent on beta adrenergic receptors and are, therefore, not well controlled by Phenoxybenzamine or Phentolamine. Propranolol is the agent of choice to deal with these problems. It has proved very helpful during the operation. Unless tachyarrythmias are a problem, the drug need not be given until just before operation. From our experience, we conclude that the operation is far less taxing on the patient and on the surgeon after adequate preoperative blockade with Phenoxybenzamine and intraoperative use of Propranolol.

The Operative Approach

The optimal operative approach is not universally agreed upon. The general principle is that the surgeon is obligated to investigate all regions in the abdomen which might potentially harbor a pheochromocytoma. These include the suprarenal areas, the para-aortic and para-iliac retroperitoneum, the bladder and the ovaries. To accomplish this exploration it is generally considered that an abdominal-transperitoneal approach is to be preferred, through either a midline or a subcostal incision. The abdominal approach does provide satisfactory access to both adrenals and all other sites of potential pheochromocytoma. There are disadvantages. For one, the patients have more prolonged postoperative ileus. Exposure of the adrenals from the anterior approach requires extensive retroperitoneal dissection; under the liver and vena cava on the right, and under the pancreas close to the spleen on the left. These tumors are always quite vascular and some are of formidable proportions. The combination of large size, extreme vascularity, and difficult exposure can lead to excessive blood loss and prolonged operative time. A flank approach provides ready access to the adrenal region with earlier and easier control of the adrenal vessels. In selected circumstances, we have used this incision. The flank approach, of course, requires that the tumor be localized preoperatively by angiographic study. As noted above, the radiologist cannot assure the absence of additional pheochromocytomas. After removing the tumor, therefore, we open the peritoneum and palpate along the aorta and iliac vessels, the course of the sympathetic chains, the bladder, and the opposite adrenal. It should be pointed out, however, that palpation alone is imperfect from any approach. On occasion I have found it impossible to feel an adrenal mass before opening the peritoneum, even knowing from the angiogram where the lesion was located. From the flank approach it is not feasible to open the peritoneum over the opposite adrenal and this is the major disadvantage.

> A rather fragile, obese 65-year-old woman with relatively poor pulmonary functions was shown by aortography to have a nine cm tumor in the left suprarenal position. With relative ease, we removed a 315 gm pheochromocytoma from the left suprarenal region through a flank incision. The peritoneum was then opened and all areas of potential chromaffin tissue palpated. A slight rise in blood pressure occurred when the region of the right adrenal gland was compressed. After the left sided incision was closed, the patient was turned and the opposite adrenal exposed through a right flank incision. The gland proved to be normal. The procedure, from beginning to end, took four hours, an operative time no more than that required for such operations done from the transabdominal approach. The patient had a remarkably benign postoperative course.

Pheochromocytomas are generally very vascular. Lesions of this size, lying near the diaphragm behind the pancreas or the liver, can be very challenging to remove from the anterior approach. From the flank the operation is neither difficult nor bloody. At present, my policy is to approach pheochromocytomas through the abdomen in circumstances where the probability of multiple lesions is great, namely, in children or in adults with associated neurocutaneous syndromes, Neurofibromatosis, Sipple syndrome, or the Von Hippel-Lindau syndrome. On the other hand, with an adult, particularly of less than optimal operative risk, obesity or poor cardiopulmonary reserve and a large pheochromocytoma clearly identified on angiography, I prefer the flank approach. Variables to consider in deciding the approach are the probability of second lesion, the habitus of the patient, the cardiopulmonary functional status, the certainty of angiographic localization, and the size of the tumor. Either a transabdominal or flank incision is acceptable and suitable, depending upon the circumstances.

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the sixth age shifts
Into the lean and slipper'd pantaloon,
With spectacles on nose and pouch on side,
His youthful hose, well saved, a world too wide
For his shrunk shank; and his big manly voice,
Turning again toward childish treble, pipes
And whistles in his sound. Last scene of all,
That ends this strange eventful history,
Is second childishness and mere oblivion,
*Sans teeth, sans eyes, sans taste, sans everything.**

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*Shakespeare: As You Like It. II. vii. 157-166.

Metastatic Sarcoma

Combined Surgical and Immunotherapeutic Approach

Neuraminidase Treated Tumor Cells As Tumor Vaccine

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The management of patients with metastatic sarcoma is discussed. Recent work indicates that surgical removal of pulmonary metastases, especially if slow growing, prolongs survival and that immunotherapy may be of further benefit. Animal experiments have shown that small amounts of tumor may be cured by immunotherapy alone, using Vibrio cholerae neuraminidase (VCN) treated tumor cells and BCG. Recently six patients with metastatic sarcoma have been treated at the University of Minnesota Hospital by immunotherapy with VCN-treated tumor cells and BCG after surgical removal of metastases. All patients are still alive but three have developed recurrent tumor. Some of these failures may, be of a technical nature. The role of immunotherapy is still undetermined and the need for more laboratory experimentation and experience with human application is obvious.

DISSEMINATED MALIGNANCY, as evidenced by distant metastases, is often regarded as a hopeless condition. Chemotherapeutic agents are now available which singly or in combinations often cause tumor regression and give clinical palliation, although usually only of short duration. The problem of distal metastases has been approached aggressively by surgically removing detectable metastases, when the primary lesion appears to be controlled. In 1966, Edlich reviewed 26 years experience with resection of pulmonary metastases from various tumors at the University of Minnesota Hospitals.[1] While the five years cumulative survival rate was 24% for the whole group and 39% for 18 patients with sarcomas, the hospital mortality was only 1.6%. Multiple pulmonary metastases and hematogenous spread to extra pulmonary organs both detracted from the success of this procedure. Since then, improved diagnostic techniques have made it possible to detect metastases in other organs more accurately and thereby exclude patients who would not be candidates for surgical removal of metastatic pulmonary lesions.

Immunotherapy is a new form of adjuvant cancer therapy and still experimental. Moore and his colleagues reported 50% two year survival in eight patients with pulmonary metastases from osteogenic sarcoma treated by surgical excision plus active immunotherapy with autologous or allogeneic tumor cells.[2] Morton recently reported the results of surgical removal of pulmonary metastases in 60 patients, 19 of whom received adjuvant immunotherapy with irradiated autologous tumor cell and Bacillus Calmette-guerin (BCG).[†3] That study showed that patients with slowly growing pulmonary metastases benefited from surgical removal and that immunotherapy appeared to have some additional beneficial effect.

Work in our own laboratories has shown that the immunogenicity of tumor cells can be increased by exposing them in vitro to an enzyme *Vibrio cholerae neuraminidase* (VCN). Established syngeneic tumors in mice could be made to regress or totally disappear if the animals were subsequently treated with tumor cells exposed to VCN.[4] This regression was immunospecific and could be augmented by the simultaneous use of the nonspecific immunostimulant, BCG.[5] However, this form of therapy has proven to be most effective against relatively small primary tumors less than 1 cm in diameter, or following surgica reduction in the mass of larger tumors.[6] Other investigators have further shown that the murine lymphomas and leukemias regressed in animals treated with VCN altered tumor cells but, again, his was more effective if the tumor cell mass was imultaneously reduced by appropriate chemoherapy.[7,8,9] All of these studies suggest that imnunotherapy may be an effective anti-tumor idjuvant in patients who have had most or all of he clinically detectable tumor removed. Based n these data, several patients with metastatic arcomas have recently been subjected to surgical xcision of all detectable tumor followed by aduvant immunotherapy with VCN treated tumor ells and BCG at the University of Minnesota Iospitals.

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Case Reports

ase 1

The patient, a 20-year-old girl, underwent local cobalt ierapy followed by right thigh amputation for osteoenic sarcoma of the right knee, discovered in May 971. At the time of surgery there was no evidence of ietastases. In April 1972 a chest film revealed two meistatic nodules in the left lung and no other evidence f metastases. Immunological evaluation showed positive in tests to histoplasmin streptokinase-streptodornase K/SD) and mumps. Immunotherapy was started with eekly intradermal injections of BCG and in July 1972, ve metastatic nodules were removed from the left ing. The tumor cells were treated with VCN and mitoiycin C and returned to the patient in three divided oses totaling 1 x 10^8 cells. At the same time, and interittently thereafter, she continued to receive injections f BCG. These were associated with strong local reacons. One month later a chest film revealed a suscious lesion in the right lung and in two months there as visible recurrence in the left lung. In January and ebruary 1973 she underwent additional thoracotomies which time two nodules were removed from the left ng and four from the right. The cells were again eated with VCN and used for immunotherapy, along ith BCG. At this time she received a total of 21 x 10^8 CN treated tumor cells and was continued on interittent intradermal BCG injections. Three months later, May of 1973, there was evidence of recurrence in the ft hilar region. At this time her lymphocyte stimulation dex had dropped to 60, well below normal. She was ntinued on intermittent BCG injections but the lesion ntinued to grow slowly over the next six months. uring this time she lost her skin test responsiveness to eviously positive antigens and her in vitro lymphocyte mulation remained poor. Chemotherapy was initiated November 1973 but the left hilar lesion has continued increase in size and a separate new lesion has also peared in the left lung.

ise 2

This 32-year-old female underwent a forequarter amputation in 1969 for a tumor in the right axilla, diagnosed as malignant Schwannoma (neurolemmal sarcoma). Two years later a local recurrence in the amputation scar was excised and she was placed on cyclophosphatamide for one month. Six months later a wedge resection was carried out for metastases in the left lung and six months after that metastases were resected from the right lung. In June 1973 she was admitted to the University of Minnesota Hospitals for evaluation for immunotherapy because of metastases in both lungs but with no evidence of tumor in other organs. Immunologic evaluation showed normal lymphocyte stimulation. Immunotherapy was started in the form of intradermal injections of BCG and in August 8 metastatic nodules were resected from the left lung and three from the right lung through bilateral thoracotomies. The cells were treated with VCN and irradiated and she received 340 x 10^6 treated cells along with BCG daily for four consecutive days. Following that she continued to receive BCG intradermally and has continued to show strong local reaction to this material as well as strong positive skin tests to PPD, mumps and SK/SD. Stimulation of her lymphocytes with PHA has shown a *subnormal* response since immunotherapy was started. Evaluation in March 1974 revealed a nodule in the left lower lobe in an area of previously resected cluster of nodules in August 1973. In review this nodule was visible in a film from November and may represent a lesion which was missed because of small size on the previous exploration. This nodule was resected on March 22 and immunotherapy reinstituted with VCN treated cells and BCG. In addition, postoperatively adjuvant chemotherapy with Adriamycin is planned.

Case 3

This 23-year-old man underwent a left thigh amputation for osteogenic sarcoma of the femur in December 1971. Pulmonary metastases became evident on a chest film in July 1973 with two nodules in the right lower lobe and one nodule in the left upper lobe. A liver scan was equivocal but needle biopsy was negative. Immunologic evaluation included multiple skin tests all of which were negative and lymphocyte stimulation indices of 37 and 35 on two occasions, both of which are well below normal. In August 1973 bilateral thoracotomies were performed and the nodules removed from both lungs. The surface of the liver felt smooth through the diaphragm. The cells were treated with VCN and stored while the patient was started on weekly injections of BCG. In one month PPD and SK/SD skin tests converted from negative to positive and his lymphocyte stimulation index rose to 148. He was then given 180 x 10^6 VCN treated tumor cells in three doses on alternate days along with BCG, which was inoculated intradermally with a Heaf gun directly over the intradermally injected tumor cells. Following discharge from the hospital BCG injections were continued. Since then there has not been evidence of recurrent pulmonary metastases, but in March 1974 an approximately 5 x 5 cm metastatic nodule was discovered in the wing of the right scapula. This was resected locally and immunotherapy with VCN treated tumor cells and BCG is being reinstituted followed by adjuvant chemotherapy with Adriamycin.

Case 4

This 11-year-old boy underwent an exploratory laparotomy in November 1971 at which time he was found to have a mass in his gastrohepatic ligament diagnosed as a rhabdomyosarcoma. This was excised along with a positive lymph node in the same area. Ten days later he was re-explored and a partial hepatectomy was performed for a four cm tumor nodule in the right lobe of the liver. At that time there was no evidence of tumor spread to other organs, and postoperatively he was treated with actinomycin D and vincristine. In May 1972 a "second look" laparotomy was carried out with no evidence of tumor being found. Intermittent courses of actinomycin D and weekly injections of vincristine were continued until December 1972. At that time he was again explored surgically and a partial hepatic resection was carried out for a 15 x 18 cm mass, again in the right lobe of the liver near the previous line of resection and a positive lymph node was removed from porta hepatis. Postoperatively he was given 4,000r to the area of tumor resection, after which alternate courses of cytoxan and Adriamycin were started to which vincristine was later added. In July 1973 re-exploration was carried out because of evidence of epigastric mass and a large recurrence was found in the left lobe of the liver. This was resected along with a metastatic nodule on the anterior abdominal wall. Again there was no evidence of residual tumor. The tumor cells were treated with VCN for future use in immunotherapy. Postoperatively he was given 4200r to the tumor site from August to October but this course was interrupted in September when he underwent one more exploratory laparotomy for a palpable mass. This time a larger tumor was found in the mesentery of the transverse colon. A subtotal colectomy was carried out removing all identifiable tumor and the irradiation therapy was completed and followed by chemotherapy. In December the chemotherapy was discontinued and immunotherapy started with weekly injections of BCG for six weeks followed by 3 x 10^9 tumor cells along with BCG given in three divided doses. This has been followed by intermittent BCG injections for the past three months and there has been no evidence of a new recurrence.

Case 5

A 68-year-old man underwent a wide excision of an undifferentiated liposarcoma of the right thigh in 1957. During the ensuing 13 years he developed six recurrent lesions in both thighs of the same histologic type as the primary lesion. All were widely excised. In January 1974 a recurrence appeared in the left upper arm. As before, metastatic workup at this time failed to show any evidence of metastases in other organs. Immunologic evaluation included multiple skin tests of which SK/SD, histoplasmin, and mumps were positive. In January 1974 the mass was removed and the cells treated with neuraminidase and stored. The patient was started on immunotherapy receiving BCG injections weekly for five weeks and then 500 x 10^6 tumor cells along with BCG. This course is presently being continued with injections of intradermal injections of BCG every two weeks.

Case 6

This 28-year-old woman who in October 1972 wa found to have an undifferentiated sarcoma of uncertai cell type, probably fibroblastic, in the right deltoid region Metastatic workup was negative and in November 197 a right fore quarter amputation was performed. Postoperatively she did well and remained free of evidenc of metastases until November 1973, when a 6 m nodule was discovered in the left lung. Metastatic worku was otherwise negative. Immunological evaluation the included multiple skin tests, all of which including PP were negative, except SK/SD which was positive. I January 1974 a left thoracotomy was performed and 2 cm nodule was removed with a wedge resection fro the left lung. The tumor cells were treated wit neuraminidase and the patient was started on immunotherapy with VCN treated tumor cells and BCG. I addition she has been started on adjuvant chemotherap with Adriamycin. So far there is no evidence of a recurrence.

Discussion

It obviously is too early to draw any conclusion about what results will be obtainable with th combined approach of surgery and immunotherapy with VCN treated tumor cells for metastati sarcoma. Three patients have already develope recurrent disease after removal of pulmonar metastases. The recurrence in the first patien occurred in the areas of previously resected nodules which were "shelled out" rather than resected. Since then, the technique has been changed t wedge resections using a stapling device and a margin of at least 2 cm of grossly tumor-free tissue. The recurrence in the second patient als occurred in an area of a previously resected cluste of nodules and may represent a nodule which was already present but missed because of small size. In that case a lobectomy might have been the proper procedure. The recurrence in the third patient occurred in the scapula, where a small metastases is hard to detect and might have been missed on the workup at the time of resection o the pulmonary nodules, and initiation of immunotherapy. The three last cases are too recent to give any useful information about the effectiveness of immunotherapy. The impression can hardly b avoided that the same results might have been obtained with surgical resection of the metastase alone.

More laboratory experimentation and human experience with various approaches to immunotherapy are necessary to find out whether resection of metastatic sarcoma followed by immunotherapy with VCN-treated tumor cells and BCG is a worthwhile procedure. Much must also be learned about the significance of immunological responsiveness of tumor patients as indicated by immunological testing, both as a prognostic aid and to help select the best therapeutic approach for each individual patient.

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Dr. Earl Ellis

Dr. Ellis was recently honored by Elgin for 40 years of service to that community.

Malignant Tumors of the Paranasal Sinuses

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Any change in the characteristics of a long standing sinusitis or development of an initial mass, nasal obstruction or change in symptoms should arouse suspicion of a tumor and indicate a biopsy.

ALL PATIENTS TREATED for malignant tumors of the paranasal sinuses at the University of Minnesota complex between 1959 and 1971 have recently been evaluated Seventy-five patients with malignancies arising primarily in the paranasal sinuses are the subject of this discussion. Patients in whom the carcinoma was felt to arise from the palate or the nasal chamber are excluded. Those patients who had only a portion of their treatment given at the University Hospital are not included.

Historical Aspects

During the past 100 years various modalities of treatment have been utilized to manage patients with malignant tumors of the paranasal sinuses. In recent reports the five year survival rate ranges from 25-35%.[1] Historical aspects of treatment methods are particularly interesting since some of these methods are now employed for both palliation and treatment of recurrent disease.

Musgrave Woodman[2] in 1923, attributed the first surgical resection of a tumor arising on the cheek to Richard Weisman, Surgeon to King Charles II. This procedure was performed on a 28 year old man with decreasing vision in the year 1671. Lizzars in 1826, formalized the operative procedure of resection of the upper jaw and advocated rapid surgery for safety and less suffering for the patient. Mr. Woodman resected a large maxillary sarcoma from a 67-year-old man in 1879. One of the most famous maxillectomies was performed on President Grover Cleveland in 1893.[3] Because of the financial difficulties in the United States at the time, it was felt that any rumor of Mr. Cleveland's ill health would cause further financial difficulties. Thus on a yacht in Buzzard's Bay off the coast of Massachusetts he underwent resection of the left-upper jaw and a portion of his soft palate for a sarcoma. A prosthesis was made at the time and inserted immediately by a dentist. His postoperative course was so satisfactory that he was able to give a speech within a few weeks. He completed his term, and helped to stabilize the United States gold currency.

In 1911, William Clark[4] reported on the experience with electrodesiccation and electrocoagulation of maxillary tumors, but did not report his end results. Among 57 cases of cancer of the jaw and cheek seen at the Mayo Clinic[5] in 1917, there were only 25 patients who were possible candidates for surgery. Joseph Bloodgood[6] in 1919 advocated electrocautery combined with surgery under light chloroform anesthetic for removal of tumors in the upper jaw. He emphasized repeated surgical attacks on the tumor.

In 1929, Douglas Quick[7] advocated the combination of surgery, radium and x-ray therapy. It is interesting to note the extent of disease in the patients he saw. Seventy-three percent had involvement of the cervical nodes on presentation. Fifty-nine percent had prolonged courses of treatment before the diagnosis was made and 45% had undergone previous local operations.

During the period of 1930 through 1945, radiation therapy came to be the most prominent method of treatment. This was because of the failure of surgery to control the local disease at the base of the skull and prevent local recurrence. Edgar Frazell[8] reported in 1955 a large series from the New York Memorial Hospital. By 1963, Frazell and Lewis[9] published data on 416 patients treated for carcinoma of the nose and paranasal sinuses between 1935 and 1954. Their reports recommended surgical resection. In 1959, Tabb[10] analyzed 81 cases and became a proponent of radical surgical resection and described his surgical technique. He recommended post operative radiation therapy to the limit of tolerance. Shaw[11] in 1965, discussed the combined use of surgery, radiation and chemotherapy by infusion. He utilized both super voltage (cobalt 60 or linear accelerator) and intracavitary irradiation (8-10,000 rads at 0.5 cm in 10-14 days).

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Another important development was the work of Smith, Klopp and Williams,[12] who in 1954, reported en bloc resection of the frontal, ethmoid and maxillary sinus with the cribriform plate. Ketcham,[13] et al. reported 19 cases of the combined operation in 1963. They included a complete discussion of the complications encountered in this procedure in another paper in 1966,[14] by which time they had performed a combined intracranial resection on 33 patients with a 61% three year survival and a 7% operative mortality. Their series had grown to 54 cases by 1973.[15]

Experience of Treatment

Methods of treatment have varied over the years at the University of Minnesota. Before 1956 radical surgery was usually the only form of treatment. From 1956 until the late 1960's the primary treatment was irradiation with surgery reserved for hose patients in whom there was biopsy proof of persistence, or in those in whom a later recurrence was felt to be resectable. Treatment modalty discussed in this paper is primarily for antral or maxillary squamous cell carcinoma which ormed the majority of these tumors. Early in his series the treatment consisted of a full course of radiation therapy, usually 6,000 to 6,500 rads, given over a period of six weeks, followed in six weeks by a Caldwell-Luc type of operative proedure with creation of a permanent antrostomy. f tumor was found, the patient underwent a radial maxillectomy. If no tumor was found following the radiation, the patient was followed carefully or possible recurrence.

This treatment plan was changed when patients were found to have recurrent tumor which was requently no longer operable when discovered. Now the full extent of tumor is determined by hysical examination and radiological evaluation. This includes polytomography of the base of the skull, the pterygoid plates and posterior and lateral walls of the sinus in addition to routine radiography. Complete evaluation is made for any evidence of distant metastases. The criteria for resectability were established to be as follows:

1. No evidence of distant metastases;
2. No extension into the nasopharynx;
3. No erosion of the pterygoid plate or other evidence of involvement of the base of the skull or no definite erosion of the posterior wall;
4. No involvement of the posterior ethmoid sinuses or sphenoid sinus.

Patients with a squamous cell carcinoma have a full pre-operative course of irradiation therapy followed in three weeks by maxillectomy. At the time of maxillectomy, presistent tumor encroachment upon the orbital floor is used as the criteria for orbital exoneration. Variations of this method of treatment are then utilized for cylindromas, adenocarcinomas and sarcomas. These tumors will be discussed separately. Radioresistant tumors are treated by radical surgical resection. Non-resectable tumors are treated with palliative irradiation therapy.

Because the line of resection for a maxillectomy is the anterior ethmoid cells, tumor involving these areas requires a different approach. The complete extent of the tumor is determined clinically. This includes preliminary treatment of co-existing sinusitis secondary to an obstructive lesion. Polytomography of the cribriform plate and ethmoid cells as well as the sphenoid region is performed. If the tumor is felt to extend into the cribriform plate, consultation is obtained from neurosurgery and if possible, a combined craniofacial resection would be performed. Involvement of the posterior ethmoid cells or the pterygomaxillary fossa precludes surgery in these patients.

Clinical Findings

The majority of malignant tumors occur in the maxillary sinus and most are squamous cell carcinomas. Etiological factors have been reported by numerous authors and frequently there is an association of pre-existing chronic sinusitis. This history of a sinusitis as well as swelling over the side of the face was the most common presenting symptom in our series. A history of sinusitis may be present for 10 to 30 years before the diagnosis of malignancy is found. In certain areas of Great Britain, adenocarcinoma has been reported to have a high incidence in furniture workers exposed to hardwood dust.[16] This was not a factor in our cases. Smoking has not been reported to be an etiological factor. Seventeen of the 44 patients with squamous cell carcinoma of the antrum in this series smoked more than one pack of cigarettes per day for several years. Noticeably absent as a symptom in this study was pain. It did become a very important feature however, as the disease progressed. Four patients who complained of pain attributed it to a local injury.

Results of Treatment

The results of treatment are divided according to the type of tumor and according to extent and location of disease. A TNM classification presently exists for sinus cancer but it is not as workable as the system which exists for pharyngeal and laryngeal tumors.

As expected, patients with early tumors have the best prognosis, while those with tumor extending into the pterygomaxillary fossa, the base of the skull or the ethmoid area had the poorest prognosis. The latter patients had unresectable disease when initially seen and were given palliative radiation therapy. With proper shielding of the ey there were no major problems associated with th high dose of radiation therapy given. Intracavitar radiation was given in six cases with recurren tumor and was a useful adjunct to cobalt therapy.

Squamous Cell Carcinoma

The results of 44 patients treated for squamou cell carcinoma are presented in Table 1. It i important to note the excellent result of three pa tients in whom the tumor was completely confine to the maxillary sinus and who did not have bon erosions of the sinus wall. Patients with tumo extending out of the sinus "box" onto the palate alveolar ridge, cheek and orbital area had a poore prognosis but were still amenable to successfu treatment. It was this group of patients who mos commonly developed cervical metastases. Thos in whom no surgery was performed because o extension of the disease into the pterygomaxillar fossa, pterygoid plates and base of the skull us ually died within one year of the time of diagno sis. Almost all recurrences of tumor in this serie were within two years of diagnosis. There wa only one recurrence after three years (Figure 1 and 2).

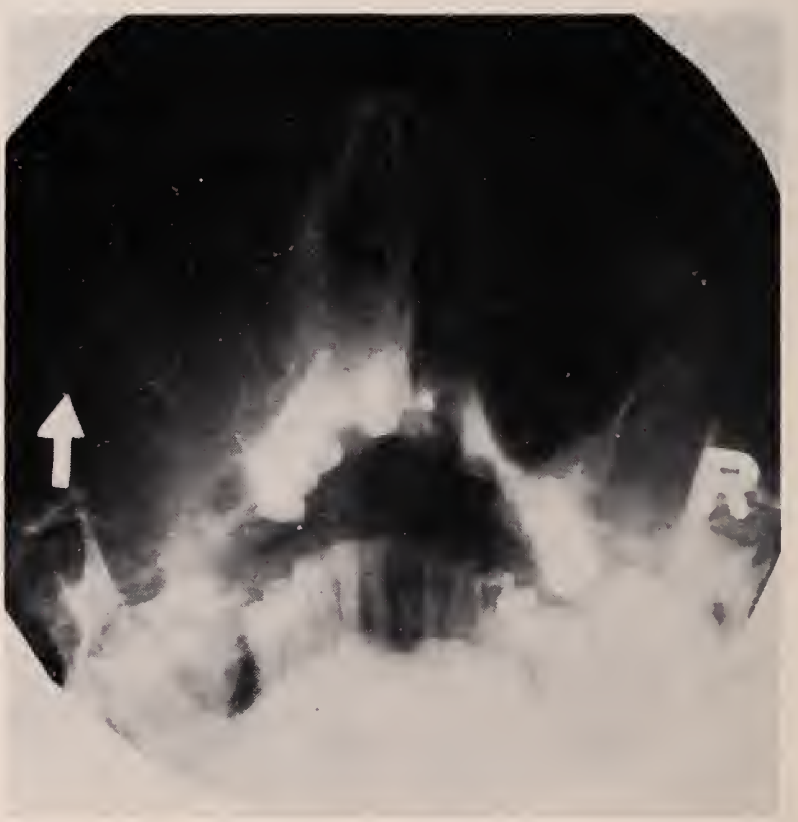

Fig. 1—Mass in the left nasal cavity, clouding of the left maxillary sinus, sphenoid sinus and ethmoid air cells. There is bony destruction of the walls of the left maxillary sinus.

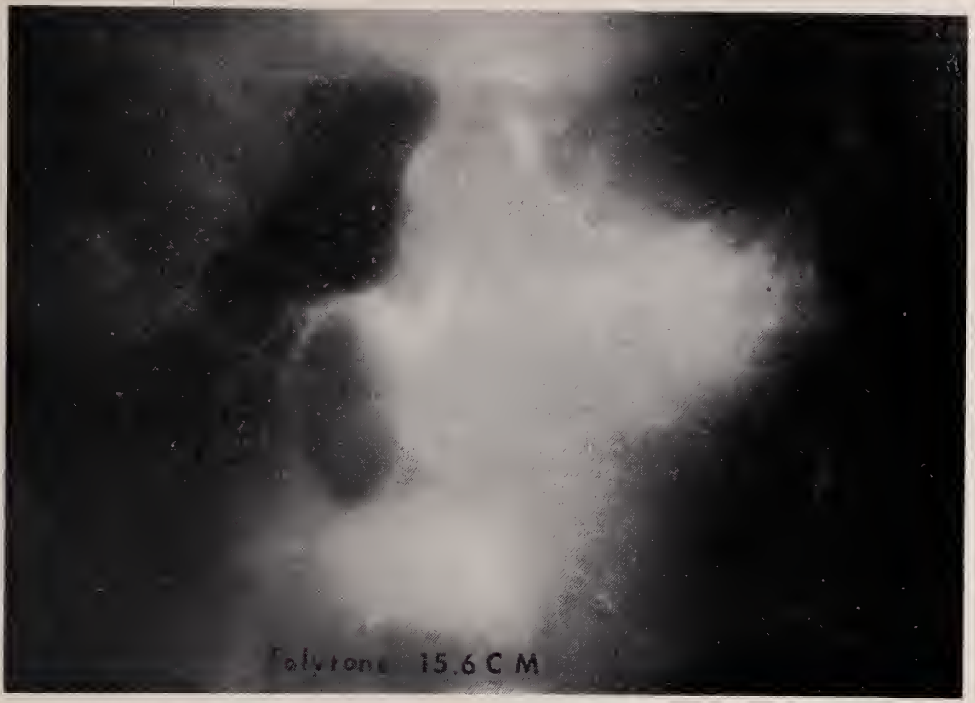

Fig. 2—Polytomography of the base of the skull reveals erosion of the pterygoid plates, extension into the medial portion of the greater wing of the sphenoid.

TABLE 1

Squamous Cell Carcinoma of the Maxillary & Ethmoid Sinuses
(44 patients)

Total # of Patients	Treatment	Cervical Nodes	Alive 2 yrs.	Alive 5 yrs.	Died Tumor	Died Other
Limited to the Maxillary Antrum						
3	Radiation—2	0	2	2	0	0
	Radiation and surgery—1	0	1	alive over 3 yrs.	0	0
Maxillary Sinus Extending Onto Alveolar Ridge, Cheek, Orbit or Palate						
23	Radiation—14	4	4	3	10	0
	Radiation and surgery—9	1	7	4	3	2
Maxillary Sinus Extending to Pterygoid Plates, Posterior Wall						
6	Radiation—5	0	2	0	3	0
	Radiation and surgery—1	1	1	0	0	0
Maxillo-ethmoid						
12	Radiation—10	1	1	0	10	0
	Radiation and surgery—2	0	2	2	0	0

Adenocarcinoma

There were 13 patients with primary adenocarcinoma of the maxillary and ethmoid sinus. Treatment for this group was primary surgical resection. Recurrent or unresectable disease was treated by radiation therapy. Results of treatment in this group are shown in Table 2. Whereas recurrence of squamous cell carcinoma would most frequently appear within one year, patients with adenocarcinoma would live with the disease or have a delayed recurrence up to 10 years after the time of diagnosis. Two patients listed in the table have recurrent disease but have survived five years.

Various types of adenocarcinoma were found to involve the maxillary and ethmoid sinuses. Papillary adenocarcinoma occurred in the superior nasal area and ethmoid sinus. It has a slow rate of growth and causes very few symptoms except nasal obstruction and epistaxis. Adenocarcinoma of the cylindroma type (adenocystic carcinoma) and mucus producing adenocarcinoma appeared most frequently in the maxillary sinus.

Four of the patients had cylindroma of the maxillary sinus. All but one presented with pain and headache. Their ages ranged from 34 to 61. The disease was generally very extensive when initially seen. Treatment was surgical resection if possible and radiation therapy for unresectable tumors. The excellent initial response to surgery or irradiation of a cylindroma has previously been reported.[17,18]

Only one of our four patients with cylindroma was amenable to surgical resection. Unsuspected malignancy was found in the pterygoid fossa. She died one year later with widespread metastases including the lung, liver, heart, adrenal and bone marrow. The second patient developed a secon primary cancer of the breast and generalized m tastases. The third patient lived two years befo dying of intercranial extension. The fourth on a 34-year-old man with a cylindroma of the rig maxillary sinus, had a positive left subdigastr node. He developed a left serious otitis medi paresis of the fifth cranial nerve and decrease vision in the left eye. A carotid arteriogra showed extension into the temporal fossa. He ha an initial good response to radiation therapy an died six years later with extension to the brain.

Cylindromas of the maxillary sinus frequent have a rapidly progressive course in contrast to th somewhat prolonged course of those arising fro the palate or a major salivary gland. Cylindroma may extend along nerve sheaths and they ma extend submucosally. This submucosal extensio frequently spreads beyond the limits which woul be considered an adequate margin of resection f any other type of tumor. Presently, prior to co sidering the patient for surgical resection, w perform biopsies of normal appearing tissue several locations very distant from the obvio tumor. Finding such tumor extensions makes o erative treatment inadvisable.

Sarcoma

There were four patients with primary sarcom of the paranasal sinuses. Treatment has been su gical resection. Three of these patients underwe a combined approach of anterior craniotomy wit resection of the cribriform plate. The younge patient was a 21-year-old woman with a chondr sarcoma of the right frontal and ethmoid sinuse Combined approach included a radical ethmoide tomy, removal of the crista, cribriform plate an orbital roof. She is now six years post surger

TABLE 2

Adenocarcinoma of the Maxillary and Ethmoid Sinuses

	# of Pts.	Treatment	Alive 2 yrs.	 5 yrs.	Died Tumor	 Other
Maxillary Sinus*	8	Rad. Therapy— (2 pts.)	1	0	2	0
		Surgery with postop rad. therapy— (6 pts.)	4	4	2	0
Ethmoid Sinus	4	Surgery	4	4	1— (at 10 yrs.)	0
Maxillo-ethmoid	1	Radiation— (extensive tumor	0	0	1	0

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*Four patients with cylindroma not included.

without evidence of recurrence. Another young man had a chondrosarcoma of the left ethmoid and is now five-years postsurgery. One woman with a fibrosarcoma of the ethmoid, frontal and maxillary sinuses is now four years post surgery. Radical maxillectomy has been performed on a 26-year-old man with an osteogenic sarcoma of the maxilla and he is now seven years post surgery without evidence of recurrence.

Plasma Cell Cytoma

Plasma cell cytoma or extramedullary plasmacytoma is an unusual tumor felt to be related to multiple myeloma. These tumors appear primarily in the upper airway. The prognosis is better than that for multiple myeloma and long term survivals have been reported.[19] Treatment has been both radiation therapy and surgery, with approximately equal results. There were three patients with a plasma cell myeloma of the maxillary sinus. Ages ranged from 45 to 73 years. These patients presented with nasal stuffiness and one patient had fullness of the palate. Only one patient had a history of chronic sinusitis and nasal polyps. One patient died from multiple myeloma six years after onset of treatment with radiation therapy. One patient died two years later free of tumor and the other patient is living free of disease.

Miscellaneous Tumors of the Maxillary Sinus

This group of patients presented with no distinct characteristics which would differentiate them from other types of malignancies. A patient with malignant melanoma with erosion of the posterior maxillary wall on presentation has no evidence of tumor four years following a full course of radiation therapy. A patient with a reticulum cell sarcoma of the right maxillary sinus had a full course of radiation therapy and although he developed no local recurrence, he developed systemic disease and died four years ater. A patient with a primary lymphoma of the eft maxilla is free of tumor three years after radiation therapy. One 82-year-old woman with a large undifferentiated malignant tumor of the maxillary sinus responded to a full course of adiation therapy. She has no evidence of recurrence of tumor but has had persistent chronic inusitis for three years.

Malignant Tumors of the Frontal Sinus

Frontal sinus malignancy is so uncommon that a general pattern for treatment has not yet been established. A combination of radiation and surgical resection has been recommended by Brounson and Ogura.[20] We have had three patients with primary malignant tumors of the frontal sinus: two with squamous cell carcinoma and one with cylindroma. The presenting symptoms were identical to those of a mucocele. The x-ray picture was also compatible with a mucocele.

The patient with cylindroma developed proptosis of the right eye and swelling of the forehead. Radiographs revealed bony mottling of the right frontal bone and absence of floor of the frontal sinus. Surgical resection through a coronal scalp flap and craniotomy was attempted but only subtotal resection of the tumor could be performed. The tumor was adherent to the dura. The patient developed pulmonary metastases and died eight months later. On postmortem examination the tumor was found to extend to the dura, skull, left eye, pituitary gland, lungs, diaphragm and adrenal glands.

One patient had a combined surgical resection of a frontal squamous cell carcinoma and is alive three years later without recurrence. The second patient with squamous cell carcinoma died of underlying renal disease while undergoing radiation therapy treatments. Autopsy showed erosion of the anterior fossa by the tumor.

Combined Surgical Approach

The combined anterior fossa craniotomy with facial resection was developed by Smith, Klopp and Ketcham.[12] The procedure of a combined approach is indicated for any tumor arising in the maxillary or ethmoid sinus, involving the anterior ethmoid cells and extending to the area of the cribriform plate. A tumor arising primarily in the nasal vault and extending into this region could be resected by this approach. We have utilized this procedure for malignancies involving ethmoid sinuses extending to the cribriform plate and not involving the posterior ethmoid cells. Seven patients have been treated in this manner, six have been followed for three years.

When the cribriform plate is eroded, surgery is not performed. Erosion of the cribriform plate is difficult to determine even in polytomography because of the existing fenestrations for the olfactory nerve.

The initial portion of the procedure is performed by a neurosurgeon. He approaches the crista and cribriform plates through an anterior craniotomy and outlines with a chisel the area which will then be resected from below. This also affords an opportunity to check for dural involvement or intracranial extension which would indicate nonresectability. After elevation of the dura the line of resection is established to extend over all bones felt to be involved by previous examination. The frontal sinuses are exenterated and utilized as a line of dissection. Enough of the floor of the anterior cranial cavity must be maintained to support the frontal lobe of the brain. This wound is closed and a standard radical ethmoidectomy or ethmoid maxillectomy is then performed using a modified Weber-Ferguson incision. The incisions made by the neurosurgeon facilitate the procedure by pre-establishing the limits of the upper portion of the resection. The wound is then closed in the standard manner with a split-thickness skin graft of the cavity, packed with an antibiotic impregnated gauze. The packing is removed in one week and the patient is maintained on prophylactic antibiotics.

This procedure has had fewer complications than would be anticipated by the fact that a direct pathway from the oral cavity to the dura has now been created. No patient has developed post operative meningitis.

Summary (Tables 3, 4, 5)

Treatment results appear to be related directly to the early recognition of the disease. Early diagnosis is difficult, because signs and symptoms are similar to benign disease and there is frequently a history of long term sinusitis pre-existing the development of malignancy.

Unilateral sinusitis that does not seem typical requires biopsy by antrotomy, usually a Caldwel Luc operation. A nasal antral window does n always provide adequate visualization and roo for palpation of the sinus walls. For the front sinus a small trephine opening is sufficient f biopsy. Tumors in the ethmoid area can usual be biopsied through an intranasal approach. Pol tomography has become invaluable in determini the extent of tumors. When a mass has erode into the sinus wall, onto the palate or aveol ridge, or has extended into the pterygoid fossa, may still be possible to provide palliation with good two-year survival. The five-year surviv rates are extremely poor. In order to improve t 35% survival rate, earlier recognition of the tumors is necessary.

TABLE 3

Primary Presenting Signs and Symptoms
(Squamous Cell Carcinoma of the Paranasal Sinuses

Swelling over cheek	12
Mass depressing palate	7
Chronic sinusitis	9
Nasal obstruction	5
Exophthalmos	5
Nasal polyps	3
Cranial nerve paralysis	2
Rhinorrhea	1

Note the absence of pain as the primary complai

TABLE 4

Patients Developing Second Primary
Malignant Tumors (6/74)

Squamous cell carcinoma of larynx
Carcinoma of the bladder
Carcinoma of the pancreas
Adenocarcinoma of the stomach
Adenocarcinoma of the prostate
Adenocarcinoma of the breast

TABLE 5

Postmortem Findings (12 of 74 patients)

Extension to middle cranial fossa
Extension to anterior cranial fossa
Pulmonary metastases
Inflammation of pia arachnoid, no tumor
Local tumor only without intracranial extension
Carcinoma of pancreas } Second primary
Carcinoma of stomach }

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Laetrile

Unproven Methods

There has been an increasing amount of publicity concerning the use of Laetrile (also known as amygdalin and vitamin B17) in the treatment and prevention of malignant disease. Continued use of B17 is said to guarantee prevention of cancer. Responsible medical agencies in the United States have failed to find any objective evidence that this material is of any use in the treatment of malignancy.

Amygdalin is found in the seeds of many fruits, one of the most commonly referred to is the seed of apricots. It has been referred to at intervals since the 1920's but has gained increasing publicity recently due to its use in the treatment of cancer at several clinics in Tijuana, Mexico, and also in the Philippine Islands, Canada, and Europe.

Promoters claim that the action of Laetrile is due to release of hydrogen cyanide within the cancer cell by action of Beta-glucosidase on amygdalin, and claim that the action of the hydrogen cyanide is augmented by benzaldehyde which s also released from amygdalin by the action of Betaglucosidase.

In the early 1950's Laetrile was investigated by the California Medical Association. Their studies revealed no benefit from the drug in the reatment of patients with cancer. At present it is a violation of law to prescribe or utilize Laetrile or the treatment of malignancy in the United States. Recent review of cases purported to show effects on malignancy by treatment with Laetrile by the California Medical Association have again resulted in a finding of no objective evidence of benefit. The National Cancer Institute and the Sloan-Kettering Institute have recently done animal studies which also failed to show evidence of anti-cancer activity in recognized animal tumor systems. An unofficial report of early data from the Sloan-Kettering Institute received wide publicity claiming to show benefit in animal tumor systems. The Sloan-Kettering Institute has subsequently indicated that upon completion of the study and analysis of the data, there is no evidence of beneficial effects.

Promoters of the drug also claim that it is virtually nontoxic to human beings. It is well known that intravenous administration produces a transient fall in blood pressure. There is little, if any, information available on animal or human toxicity studies at the present time.

Laetrile has been used in combination with other accepted anti-cancer agents, but there is no information to indicate whether or not it accentuates toxicity of such agents.

Scientific investigation fails to support the theoretical basis proposed for the use of Laetrile and repeated investigations have failed to show that Laetrile is of any benefit in the treatment of tumors either in animals or humans.

John H. Brown, M.D.
Chairman, Unproven Methods Committee
Minnesota Division, American Cancer Society

Minnesota State Board of Medical Examiners

Minnesota State Board of Medical Examiners—Plaintiff vs Henry H. Unruh—Defendant.

The action came for trial without a Jury in the City of Windom, Minn., on the 30th of November, 1973, The Honorable Harvey A. Holtan, Judge presiding.

Finding of Fact

On or about December 1, 1972, the Defendant, in response to a letter from the Roy Gerlock family of the State of Wisconsin requesting medical advice and assistance, wrote to said family from his residence in Mountain Lake, Minnesota. Defendant in said communication prescribed for the Gerlock family the internal use of Hammers Baking Soda in connection with a prescribed diet of certain vegetables, liver, fruits, fruit juices, natural cheese, nuts and seeds as a remedy or treatment to stop or otherwise ameliorate a human cancer as well as a benefit to the general health of persons whether well or ill. The Defendant also prescribed the internal use of pine needles, twigs and vitamin A,C and E as a treatment or remedy for emphysema.

He also prescribed and recommended certain mineral and vitamin substances as a treatment of cancer and emphysema, to be purchased from the Anabolic Foods, Inc. of Glendale, Ca. The company deals only with members of the healing professions and will fill patient's orders only as an accommodation to the patient's doctor. The defendant included with his communication to the Gerlocks a patient order form and postage paid envelope to the company's distributor in Minneapolis, indicating on the form the substances to be purchased. He signed his communication "Dr. Henry H. Unruh."

The defendant is not and never has been licensed to practice medicine in the State of Minnesota or in any other state nor has he ever held a medical degree from any accredited college, university or school. At one time he was authorized to practice the art of massage in some other state. The Defendant is a high school graduate, had one year of junior college and has taken several correspondence school courses from schools in Texas and Illinois in the field of naturopathy and claims to hold eleven degrees or certificates in such and related fields.

The defendant requested payment of a fee for his services in an unspecified amount; no evidence was introduced to indicate whether or not a fee was ever paid by the Gerlocks to the Defendant.

The defendant in 1958 in Morrison County District Court, Little Falls, Minnesota, was convicted for violation of the Minnesota Basic Science Act. In December 1958 Defendant was convicted in the State of South Dakota for a violation of their laws covering the regulation of the healing arts. Defendant was found in contempt of Court in South Dakota in April 1960 for continuing to engage in proscribed medical practices and was again found in contempt of Court in said state in June 1964 for continuing to engage in some type of medical practice and was again in November 1965 found in contempt of Court in said state for continuing to engage in such proscribed practice. The Defendant is presently and has been since 1969 involved in various capacities, generally as a sales person, in companies selling natural and organic foods and fertilizers and supplements for human as well as animal consumption.

That Defendant was engaged in the practice of medicine and the continuation of such practice will be injurious to the public health and welfare.

IT IS HEREBY ADJUDGED AND DECREED.* That Plaintiff is entitled to Judgment permanently enjoining the Defendant, Henry H. Unruh, from practicing medicine without a license in violation of the laws of the State of Minnesota, including Minnesota Statutes Chapter 147.

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*Record of judgment editorially abbreviated—Editor.

Submitted by Bror F. Pearson, M.D., Secretary-Treasurer, Minnesota State Board of Medical Examiners.

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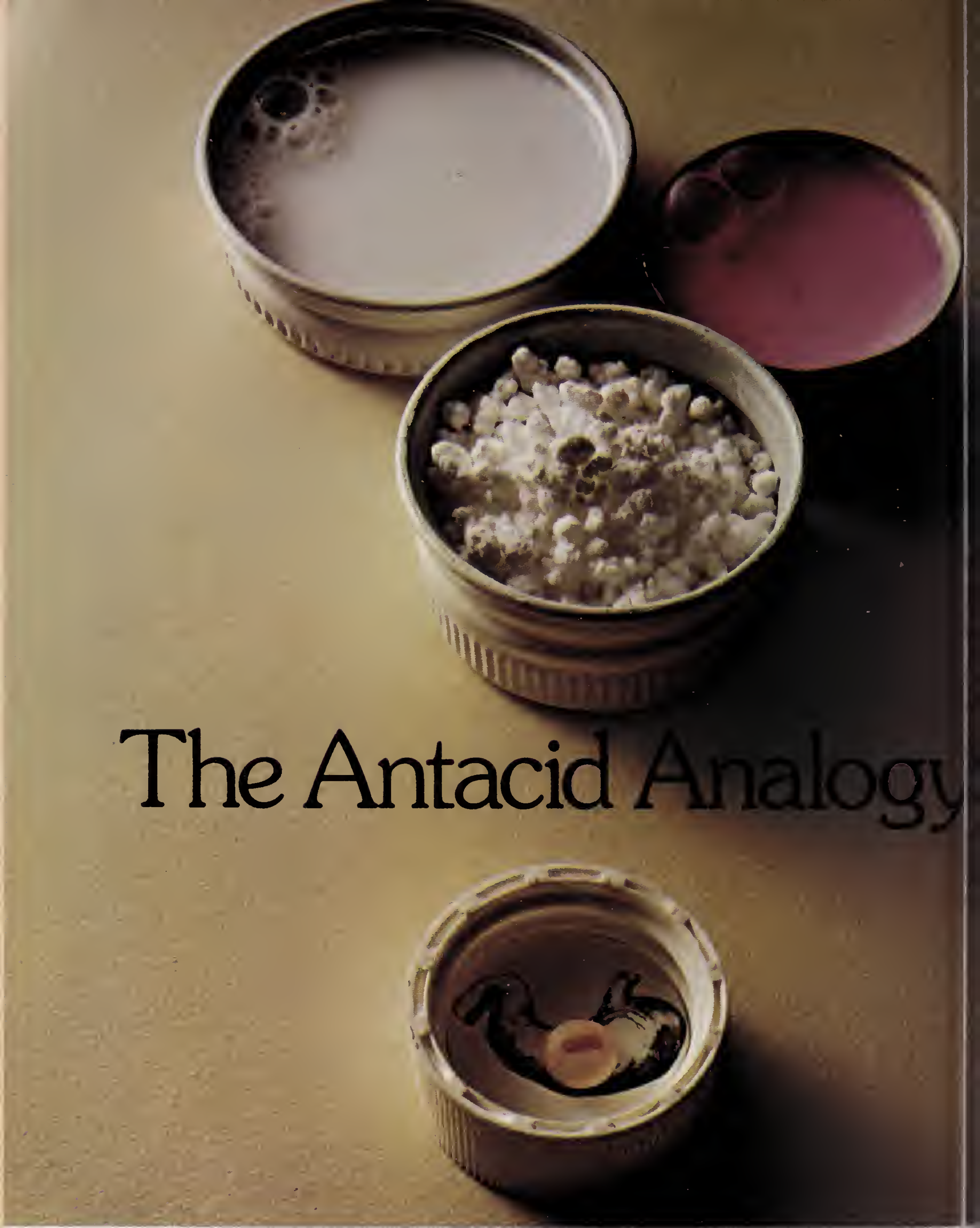

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*Innes, I. R., and Nickerson, M., in Goodman, L. S., and Gilman, A. (editors): The Pharmacological Basis of Therapeutics, ed. 4, New York, The Macmillan Company, 1970, p. 537.

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Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

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*Serum Potassium Level Drops During Long-Term Exercise, *Medical Tribune*, July 4, 1973.

†No implication that 'Dyazide' is useful in preventing K⁺ loss in athletes is intended.

Editorials

Accountability

Most of us have had the experience of attending a medical meeting; particularly a national meeting, and have felt the pride that comes with announcing that we are from Minnesota. There are many reasons for being proud of medicine in Minnesota, but as guest editor, I would like to add another, namely the overwhelming response to a call for papers for Minnesota Medicine.

A dedicatory scroll located in the entry to the Masonic Memorial Hospital states in part:

> *". . . A Committee on Organization composed of thirty Masons, planned and directed the Statewide Campaign. Six regional and 32 district committees functioned through Blue Lodge workers. Appoximately 3500 Masons worked in the fund raising activities . . . Members of the Masonic fraternity were visited by workers who explained the need for this hospital and accepted voluntary contributions from some 35,000 individual Masons and their families."*

This issue is being devoted to progress in Oncology at the University of Minnesota. In a sense, the number and the quality of the papers submitted represent a public accountability; a public expression of thanks to those individual Masons and their families who demonstrated their faith in Minnesota Health Sciences by sending their dollars for the construction and maintenance of the Masonic Memorial Hospital.

It is also a pleasure to announce that this faith has been further justified by the recent designation of the University of Minnesota as a cancer research center.

John B. O'Leary, M.D.
Guest Editor

Oncology

CANCER WILL EVENTUALLY afflict one in four Americans now living, that is, 53 million persons. In 1974, there will be 655,000 patients with newly diagnosed cancer, not including superficial skin cancer or carcinoma-in-situ of the uterine cervix. In this same year, more than one million Americans will be under medical care for cancer; 355,000 will die of the disease. Of every six deaths from all causes in the United States, one is from cancer. Taking into consideration the loss of income due to illness from cancer as well as the actual cost of medical care, the annual cost of cancer to this country exceeds 15 billion dollars. This makes the 600 million dollars annual expenditure for cancer study small indeed. Such figures emphasize that the cancer problem is a formidable challenge to medical science.

During the past 40 years, significant changes in the course of some cancers have occurred as a result of advances in science. It became clear that early cancer detection is an effective means of attacking the cancer problem. This has resulted in a rapidly declining mortality from cancer of the uterine cervix. Patients with treated stage I breast carcinoma have a survival comparable to the population without cancer. In other cancers, the impact of the medical advances has not yet reached a sufficient volume of people to alter the overall statistics.

Other unfavorable data are of concern to many. A striking increase in carcinoma of the pancreas cannot be explained. The phenomenal increase in lung cancer in males can be explained; and now the increase is occurring in women. If cigarette smoking was prohibited, 17% of deaths due to cancer would be abolished.

Practically all cancer experts agree that a large number of cancers are due to environmental factors. In Japan and Africa the incidence of colon and rectum cancer is low. When these people come to the United States to live, the incidence of these cancers increases and tends[2] to approach that of other Americans. Conversely the high incidence of cancer of the stomach in Japanese and Norwegians decreases when these people live in our country where the declining incidence of this neoplasm remains unexplained.

The injury from external causes and our way of life is emphasized by the association of asbesto fibers and mesotheliomas, vinyl chloride in aerosol sprays and angiosarcoma of the liver, solvent and leukemia, cigarettes and lung cancer, amon others. Prevention of exposure to carcinogeni agents and awareness of genetic factors coul significantly reduce the risk of cancer. To mak the public aware of these factors, physicians mus actively participate in public education.

The treatment of cancer began by surgical removal of tumors. The development of radiatio therapy improved the therapeutic results. Wit the advent of cancer chemotherapy, notable progress has been made in 35 years. Initially beginnin as a form of palliative therapy, the destructio of tumors by hormones and chemicals soo proved to be a means of controlling cancer. Mor recently these agents have proved to be potentiall curative for specific widespread diseases (e.g testis cancer, choriocarcinoma, Burkitt's lymphoma). Now multi-modal therapies offer eve greater potentials. For example, radiotherapy, surgical amputation and postoperative chemotherapy as combined treatment of primary osteogenic sarcoma has resulted in impressive disease-free survivals. Studies of other neoplasms will be approached in a similar manner.

These multi-modal therapies require the coordination of many professional experts. To meet this demand, the specialty of oncology developed. Oncology (from the Greek *onkos,* tumor) is the branch of medical science that deals with the study of tumors. Although all areas of medicine have been involved with cancer, the evolution of Medical Oncology as a new subspecialty of internal medicine has emphasized the demand for physicians specially trained in the management of patients with cancer. The surgical oncologist, radiation oncologist, and pediatric or medical oncologist interphase as a team in the care of the patient. Under all circumstances, one of these team members acts as the captain in the overall coordination of the team and the many supporting health professionals required in the management of a specific patient with cancer. These experts act as consultants to the family physician who bears the enormous task of the long term management of the patients with cancer.

To support and improve treatment methods, asic and applied research comprise essential omponents of the progress in cancer. The study f the immunologic processes in the development f disease and aging is a promising lead. Coniderable fundamental data is required before ffective clinical application of immunotherapy an be employed. Conclusive proof that viruses ause human cancers is still a goal of investigaors. While a virus may not be the cause, it may e triggering a mechanism required in the deelopment of cancer cells. Hence, the study of he cell and its processes constitutes a sound asis for continuing research.

The study and management of patients with ancer is a model for the teaching of students f health professions. Since the concepts of mangement of the cancer patient are in constant hange, the learning process is never ending. The cancer centers and oncology experts provide a focus for the ongoing educational process of the health professionals and the public.

Minnesota has been a leader in the progress against cancer; in epidemiology, cancer detection, treatment, research and education. The University of Minnesota School of Medicine and the Mayo Clinic have international recognition. The support of the Public Health services, American Cancer Society, Masons of Minnesota, and many other private groups have provided this state with exceptional health opportunities for the patients with cancer. Although the ultimate goal is to prevent or cure all cancer, the immediate goal is to bring to all patients with cancer the optimal methods for cancer detection and treatment. This can be attained with the vigorous participation of all physicians.

B. J. Kennedy, M.D.*
Guest Editor

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*Professor of Medicine, Director of Medical Oncology, Mason-Professor of Oncology and President, Minnesota Division, merican Cancer Society.

Lymphangiosarcoma

YAN, LOBER, AND KENNEDY* have reported ive additional cases of an uncommon complicaon of chronic lymphedema. All five have been een at the University Hospital since 1960, and ll occurred in women who had radical mastectmy for carcinoma of the breast.

The two cases presented in detail indicate that onsiderable time elapsed between the onset of pparently characteristic skin lesions and the acomplishment of diagnosis and definitive treatent. Woodward et al.[1] have commented on the pparent relationship of early treatment to survival. In the Mayo Clinic series the five longrm survivors who were treated by amputation veraged 5.6 weeks from onset to operation, hereas the nine patients who died following amutation averaged 24 weeks.

Prompt evaluation of ecchymosis, increased ain, or sudden increase of edema or development of purple-red nodules in the skin of an involved extremity should lead to early diagnosis and so to increased survival.

From the clinical and histologic features of lymphangiosarcoma it seems reasonable to assume that the malignant change in the hyperplastic lymphatic endothelium is multicentric and often widespread in the involved extremity. This could explain why local excision of grossly apparent lesions almost invariably fails to eradicate lymphangiosarcoma. In the past, radiation therapy has accomplished little against this disease. Chemotherapy is still in the investigative stage; but in the future it may combat systemic spread, particularly when the lesions—apparently confined to an extremity—are removed by amputation.

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Mayo Clinic

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*See page 538.

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Asymptomatic Gonorrhea

ASYMPTOMATIC GONORRHEA in the female has been publicized as one of the major problems in the diagnosis, prevention and control of the disease. The magnitude of the problem is best determined through concentrated and cooperative effort of the physician and the laboratory. In the June issue of MINNESOTA MEDICINE* is an article "Asymptomatic Gonorrhea" which describes the situation with the female in the rural area of Minnesota. There was close working cooperation between Hilfiker, his colleagues and the Division of Medical Laboratories, Minnesota State Department of Health. Accordingly, the data presented in the publication represents the ideal situation. The Table showing "No Growth Culture" does not mean defective media. poor specimen collection, improper handling, or lack of proper temperature for growth of the gonococci. Controlled studies of media for gonococci which I plan to publish at a later date support the interpretation that the culture medium Transgrow with the inhibitor suppressed the growth of the vaginal flora other than the gonococci. Accordingly, the statement "No growth" in essentially all cultures properly collected and incubated may be justifiably interpreted as a negative culture gonorrhea. Hilfiker et al., point out that ind criminate routine culturing for gonococcal fection among women who present themselves rural primary physicians might not be warrant The laboratory data certainly supports this obs vation. I made a similar observation after evalu ing routine vaginal cultures for gonorrhea fr women who presented themselves to the plann parenthood programs which included the cit of Minneapolis and St. Paul. Of 4,951 cultur only 0.4% were positive for gonorrhea. The e dence gives direction where our current increas efforts to stamp out gonorrhea should be exert namely the clientele which seeks help at the "Fı Clinic." "Walk-In-Clinic" and detention center

The low incidence of gonorrhea in the t female groups discussed obviously does not me that there is no gonorrhea problem. What being conveyed is the need for selective cultu properly taken by the physician and examined a reliable laboratory. This will result in a m efficient use of the physician and laboratory p sonnel time and materials, allowing for grea attention to the problem areas.

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Director, Division of Medical Laborato
Minnesota Department of He

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*Hilfiker DW et al.: Asymptomatic gonorrhea. Minnesota Med 57:503. 1974.

Fluorescein Angiography

IN THEIR ARTICLE discussing the use of intravenous fluorescein in performing angiography of the ocular fundus, Shapiro, Shapiro, and Vagstad* properly emphasize the value of this technique in various clinical entities. Fluorescein angiography can provide information in three general ways. First, it documents and makes readily visible certain morphologic alterations of the choroid and retina, particularly those involving retinal vasculature. Second, it can provide a way of observing the dynamics of retinal and choroidal circulation, and third, it may demonstrate pathologic alterations of vessel and tissue permeability.

In the first instance, alterations in the retinal vasculature (including the capillary bed) are made readily apparent since the retinal vessels, which are normally impermeable to fluorescein, are sharply contrasted against the darker background choroidal fluorescence. Even relatively small changes in the pigment content of the retinal pigment epithelium can be detected, because an increase or decrease in pigment tends to eit "mask" and make darker, or "unmask" and ma brighter, the background fluorescence emanati from the choroidal pool. By making subtle stru tural changes clearly visible, fluorescein angi raphy can provide information that helps defi certain disease processes. More important though, fluorescein angiography has forced us examine more discerningly, because we ha learned that most of the structural changes vealed with this technique can also be found careful clinical examination.

In the second instance, fluorescein angiograp has proven invaluable in studying the dynamics circulation within the retina and choroid. It provided basic information relative to ocular fl patterns and will continue to be useful in ongoi studies, particularly at the research level.

The third means by which fluorescein angi raphy can provide information is perhaps most valuable and most exciting aspect of application in eye disease. By demonstrating si of abnormal vessel-wall permeability or sites normalities of tissue permeability, fluorescein giography has helped provide a better under- nding of the pathogenesis of diseases such as nile macular degeneration and diabetic retin- athy, has helped to define more clearly clinical tities such as cystoid macular edema, which ten are difficult to recognize, has helped provide tional treatment of certain ophthalmic diseases r which therapy has previously been nonexistent ineffective (such as central serous choroid- athy), and has provided information helpful making the diagnosis of retinal and choroidal mors and inflammations.

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*Shapiro Irving et al.: Fluorescein visualization of the fundus in neurology. Minnesota Med 57:451, 1974.

However, fluorescein angiography is simply a chnique that provides another approach to the idy of the ocular fundus. Though it has passed test of time, like most clinical tests it has not ed up to all of its initial expectations. It cannot be relied upon, for example, to differentiate benign from malignant choroidal tumors, nor can it always be relied upon to differentiate pseudopapilledema from true papilledema.

Fluorescein angiography must not be regarded as indispensable for providing high quality ophthalmic care. In those instances where fluorescein studies might be helpful, clinical observation of the fundus, using a cobalt-blue filter after intravenous injection of fluorescein, can provide useful information without the need for expensive photographic equipment. For those cases where photographic study or documentation is desirable, however, angiographic studies can always be requested from any of the offices or institutions that are suitably equipped.

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Need for Single Institutional Clinical Reviews

N THIS ISSUE, John Delaney[†] has reviewed the sults of treating pheochromocytoma and David ang, et al.,[‡] have reviewed their cases of mul- le myeloma. Such reviews of disease entities nstitute an important part of each institution's ntinuing assessment of their own methods and ould be done on a recurring basis by all hos- tals. It is probably the most effective tool r continuing education available to a hospital aff.

Only during the past two or three decades ve data on various disease entities been kept in accurate enough fashion to permit compari- ns such as Kiang has made. Papers presenting statistical analysis of these types of data, are, fortunately, disparaged by some, yet decision aking in medicine should be based on a de- iled knowledge of the risks from the several urses open to the patient, and only such analy- can present these risks. Such detail must not ly be available to a physician, but must be own by him. Anytime a physician agrees to e a patient, a decision is required *at that time,* can not be postponed. The physician must her decide to treat the patient by a given ethod or not to treat him by that method *at at time.* Each of these decisions carries some k of death or disability. This decision may be made knowledgeably from an awareness of the magnitude of each risk, or it may be made by procrastination, with the Lord given the blame for a poor outcome.

Delaney reported that several of the conclusions resulting from his review were contrary to generally accepted dogma. The publication of such a conclusion is often helpful to the medical community in re-evaluating principles which may have been derived from the study of a very selected patient population or developed using now outdated methods. For all physicians, a knowledge of the results from the institution in which they themselves work, forms a far better basis for decision making than do those data published by a distant institution of national repute and unique patient population. This same principle applies to the need for intra-institutional studies of different therapeutic regimens rather than a comparison between two hospitals with different staffs and differing patients. The results from many such studies are more a product of the conditions of entry into the study than of any variation from the treatment modalities. This criticism does not apply to controlled cooperative studies between several institutions in which statistically valid data based on relevant controls are obtained. It is rather a plea for decision making from data applicable to the actual situation at hand.

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Microneurosurgery at the University of Minnesota Hospitals

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The operating microscope has been a standard surgical tool in otolaryngology and ophthalmology for two decades. More recently, the neurological surgeons have found it to be helpful in special situations. This communication is intended to present a summary of the types of neurosurgery being done at the University of Minnesota Hospitals with the aid of the operating microscope. The particular advantages offered by this type of magnification will be explained along with the description of the various surgical procedures.

Cerebral Revascularization and Arteriovenous Malformations of the Spinal Cord

JAMES I. AUSMAN, M.D., PH.D.*

STROKE IS THE most costly single disease in this country. Over one-half million people have a stroke each year and 200,000 or 60% of these people die from their stroke. Stroke is the third leading cause of death in the United States, after heart disease and cancer.[1] The causes of stroke due to defective blood supply to a portion of the brain include thrombosis, embolism, aneurysm, or hemorrhage. Although medical and surgical treatments are available for those patients with cerebral aneurysm and hemorrhage, and for one-third of stroke patients who have transient ischemic attacks as a presenting symptom complex, little but supportive care can be offered for those with a completed stroke.[1]

As a promising approach to the treatment of patients with stroke or prevention of stroke, a new procedure has been developed which will bring additional blood to the brain. Cerebral revascularization, entailing anastomosis of the superficial temporal or occipital arteries to the middle cerebral artery has been introduced and performed in the past seven years in a number of institutions throughout the world.[2,3] These revascularization procedures have been used in the treatment of patients suffering from transient ischemic attack with a related but surgically inaccessible lesion i the extra- or intra-cerebral vascular supply. Sucl patients have transient attacks of weakness, numbness, visual loss, dizziness, and memory loss; thes symptoms are associated with internal caroti occlusion, carotid siphon stenosis, middle cerebra artery stenosis, vertebral basilar lesion, multipl vessel occlusions, or stenoses, all with poor collateral supply. The procedure has been used i the acute stroke, secondary to middle cerebra embolus.

It has been used in patients with a progressin stroke which is unresponsive to anticoagulation Even more startling and still more controversial i the use of cerebral revascularization in patient with completed strokes with mild to severe neurologic deficits. Improvement in patients with apparently fixed neurologic deficits has been reported, but much debate about the value of th procedure exists due to criticisms of patient selection and evaluation.[2,3]

The procedure entails the suturing of vessel of one to two mm in diameter to the one mm cortical vessels; this is possible only with the operating microscope and neurosurgical microvascula techniques. A high percentage of patency aproaching 80% can be achieved in such anastomoses. With time the enlargement of the anastomotic channel has been documented, suggesting an adaptation to increased flow through these vessels.

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The Departments of Neurology and Neurosurgery at the University of Minnesota have undertaken a cooperative prospective evaluation of cerebral revascularization in the treatment of stroke.

Arteriovenous Malformations of the Spinal Cord

Arteriovenous malformations of the spinal cord were formerly believed to be rare but are now being diagnosed more commonly as their natural history has become more familiar and as diagnostic echniques have improved. These lesions are located predominantly on the posterior surface of he spinal cord and produce clinical symptoms by apparently diverting the normal blood supply to he cord through an arteriovenous fistula. Thus an ischemic cord is produced. These lesions may also present with subarachnoid hemorrhage.[4,5] Arteriovenous malformation of the spinal cord causes back pain and usually progresses to motor and sensory impairment to the lower extremities and eventual bowel and bladder malfunction.[4,5] The lesions are detected by large volume myelography sufficient to demonstrate the anterior and posterior aspects of the spinal cord up to the cervical region if necessary. The small volume, six cc, myelography which demonstrates only the anterior subarachnoid space often will not reveal the posteriorly placed malformations. Angiography is used to localize the malformation and facilitate removal.

Formerly these lesions were treated unsuccessfully by decompressive laminectomy, section of the dentate ligaments, and/or vascular feeder ligation, but now they are being directly removed with aid of the operating microscope.[5] Patients with the least deficit have the best chance for improvement.[5] Thus the early diagnosis is important to the prognosis. We believe these lesions should be removed as soon as they are recognized. Yasargil has removed lesions within the substance of the spinal cord with little or no residual deficit produced. These advances have converted this once incurable disease to a treatable and less disabling lesion.

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And of another thyng they weren as fayn,
That of hem alle was ther noon yslayn,
Al were they soore yhurt, and namely oon,
That with a spere was thirled his brest boon.
To other woundes and to broken armes
Soome hadden salves, and somme hadden charmes;
Fermacies of herbes, and eek save
*They dronken, for they wolde hir lymes have**

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*Chaucer, The Canterbury Tales, "The Knight's Tale," lines 2707-14.

Tumors, Aneurysms and Peripheral Nerves

Brain and Spinal Cord Tumors

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Tumors that arise adjacent to the brain stem and cranial nerves present the greatest challenge to the neurosurgeon. It is of paramount importance that the surgeon avoid injury to the delicate adjacent central nervous system tissue if one hopes to accomplish a successful removal. The operating microscope can be a significant aid in avoiding these complications. The two major advantages of the operating microscope are magnification and illumination. The magnification allows easier delineation of small nerves and blood vessels which are often adherent to the tumor surface. It may therefore be possible to separate these structures from the tumor and preserve them. If one is using the standard operating room lights or even an operating headlight, there is a problem of parallax because the light is not eminating from the same location as the surgeon's eyes. The lighting system in the operating microscope is designed to provide excellent lighting even in areas of limited exposure and one is able to avoid excessive brain retraction in order to visualize the tumor.

The advantages of the operating microscope are best illustrated by describing an acoustic neurinoma and the problems encountered in its excision. This tumor arises from one branch of the eighth nerve in the area of the internal auditory meatus. As the tumor enlarges, the seventh nerve is stretched around its capsule. With further enlargement the tumor indents the brain stem, stretches the fifth cranial nerve and can also involve the ninth, tenth, and eleventh cranial nerves. There is one treacherous problem that can arise if the anterior-inferior cerebellar artery becomes stretched around the tumor capsule. This artery supplies the brain stem and if it is damaged the consequences may be disastrous. This tumor, although benign histologically, is extremely difficult to remove because of the surrounding delicate and vital structures. A major goal in removing this tumor is preservation of the seventh nerve, which may be stretched into tiny individual fascicles. It is difficult to see a nerve such as this in less than optimal lighting conditions and without magnification. The operating microscope allows us to delineate the nerve on the tumor capsule and gently separate it from the capsule as the tumor is being removed. Similarly, the anterior-inferior cerebellar artery can be better visualized and damage to it avoided. Although loss of the seventh nerve is not a life threatening situation, it is certainly an unfortunate and disfiguring complication often associated with removal of this tumor. It was formerly considered that preservation of the seventh nerve could not be accomplished in cases of large acoustic tumors, but with the advent of the operating microscope, we have been able to preserve it more frequently in recent years.

The same advantages as mentioned above are present when one is using the operating microscope in the area of the optic chiasm and parasellar areas. Some spinal cord tumors have an ill-defined plane between them and the surrounding tissue and once again the lighting and magnification of the microscope can enhance their removal. The operating microscope is less helpful in tumors of the cerebral hemispheres and in most malignant tumors.

Cerebral Aneurysms

Aneurysm surgery is fraught with complications even under the best of circumstances. Although use of the operating microscope does not necessarily ensure ideal results, it can be helpful. The magnification is useful in the delineation and separation of the aneurysm from the parent vessel and its branches. Brain retraction is limited because of the ideal lighting situation. Middle cerebral artery aneurysms best illustrate the advantages of the operating microscope. These aneurysms typically arise at the trifurcation of the middle cerebral artery. This means that three important branches of this vessel are often intimately associated with the aneurysm, especially if it is a large one. Without the aid of magnificaton, one is sometimes unable to decide whether a branch is arising from the aneurysm itself or simply wrapping around the aneurysm and adherent to it. The use of magnification and microinstrumentation allows separation of these vessels from the wall of the aneurysm making it possible to delineate the aneurysm base and apply an appropriate metal clip. Aneurysm surgery is a special area within neurosurgery and the microscope does not make up for, or in any way replace the most important factor, which is the surgeon's experience.

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Peripheral Nerve Repair

The repair of peripheral nerve injuries has remained a frustrating and often disappointing area of neurosurgery. Although one can often technically reapproximate the nerve endings, the desired result of a neurologic recovery is often not achieved. We believe that the use of the operating microscope may enhance the results of peripheral nerve repair. The following four peripheral nerve problems are illustrative: (1) There is much debate regarding repair of acutely transected peripheral nerves. We believe that a cleanly transected nerve, not associated with significant surrounding tissue damage, should be repaired primarily. The nerve is prepared in standard fashion by excising any ragged edges and the severed ends are approximated. When a standard epineural repair is used with the aid of magnification, external landmarks on the nerve such as blood vessels are aligned in an attempt to establish proper reapproximation. With use of the operating microscope, one is often able to visualize the different sizes of the fascicles and therefore approximate more accurately in hopes of reconnecting the nerve as it was prior to the injury. One can use 9-0 or 10-0 suture, and connect the individual fascicles end to end so that there is no intervening gap where fibroblastic activity can take place. A stronger suture material such as 7-0 can be used to approximate the epineurium for tensile strength. (2) In delayed nerve repair, where a period of several weeks has elapsed, the microscope can also be of help. A neuroma will have formed at the proximal nerve stump and under magnification one is able to progressively excise the neuroma until good viable fascicles are seen. Although fascicles can be seen with the unaided eye, one can more readily define good fascicles from surrounding scar tissue with the proper magnification. One can then proceed with a fascicle to fascicle repair again using a fine suture. In delayed repair, one is not able to match sizes as readily because the distal fascicles will have shrunk, making it less likely to distinguish its matching partner in the proximal stump. (3) In partial nerve transections, especially if the repair is delayed, it is very difficult under direct vision to separate transected fascicles from intact fascicles. With magnification, one is able to microdissect the transected fascicles, preserving the intact fascicles much more readily. One can then repair the transected portion of the nerve as described above. (4) A fourth area of peripheral nerve surgery that has been even less successful is that of a nerve grafting. Nerve grafts are used occasionally when the distal and proximal nerve stumps cannot be approximated directly. The success of a nerve graft depends on the axon penetrating two repair sites as opposed to only one in a primary nerve repair. We have used a small peripheral nerve such as the sural nerve, and cut it into appropriate lengths to make up the gap. Using magnification one can approximate the fascicles of the nerve graft to the fascicles of the proximal and distal nerve stump. We believe this fascicular repair enhances the likelihood of the axon penetrating both repair sites. One can readily understand how this type of graft would fail if only a gross approximation of the fascicles was performed as is likely to happen if magnification is not used. Our results have been sufficiently encouraging so that we are utilizing this type of repair whenever necessary.

*How lonely we are in the world! How selfish and secret, everybody! You and your wife have pressed the same pillow for forty years and fancy yourselves united.—Psha, does she cry out when you have the gout, or do you lie awake when she has the toothache?**

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*Thackeray: Pendennis, Chapter XVI. 1850.

Transsphenoidal Pituitary Surgery

EDWARD L. SELJESKOG, M.D., PH.D.*

During the past several years, there has developed a renewed interest in the transnasal-transsphenoidal surgical approach to the pituitary gland. This rekindled interest has primarily related to the popularization of this unique surgical procedure by Jules Hardy,[1] and other surgeons who have now garnered a rather extensive surgical experience with this technique in treating pituitary tumors, as well as for hypophysectomy in selected cases of metastatic breast or prostatic carcinoma. Originally, this approach to the sella and pituitary region was popularized by Harvey Cushing, the pre-eminent American neurosurgeon of the early 20th century. Despite Cushing's generally favorable operative results when dealing with all types of intracranial tumors, the transnasal-transsphenoidal approach to the pituitary gland even in his hands carried a significant morbidity and mortality. This related to several factors including the fact that the majority of his tumors were large. Equally important was the lack of antibiotics for treatment of the potential infectious problems. As a consequence, the transsphenoidal approach to the pituitary gland fell into disrepute, and for a number of decades pituitary tumors and hypophysectomies were generally approached via the more familiar frontal-transcranial route beneath the frontal lobe.

Despite the generally favorable morbidity and mortality using the standard transcranial-frontal approach, the procedure does possess several disadvantages. These include the minor cosmetic problems related to partial head shaving, the surgical scar and bone flap, as well as the risks of wound and bone flap infection, especially due to the proximity of the frontal sinuses. There are also the risks associated with retraction and manipulation of the frontal lobe. In the hands of skilled and experienced surgeons, these problems are minimal.

With the use of the operating microscope, there developed an interest in renewing old surgical procedures. The transnasal-transsphenoidal approach to the pituitary gland naturally fell into this category. Using this technique, a number of the disadvantages of the transcranial-subfrontal avenue are obviated, including the cosmetic problems, as well as potential problems involving the frontal lobe. The major advantage of this technique is better visualization of the magnified pituitary gland or tumor. Under these circumstances, it has even been possible in cases of acromegaly, to excise selectively the adenoma and to preserve the compressed normal pituitary gland. Post-operatively, these patients have had a fall in their growth hormone levels to normal or subnormal values, along with preservation of other endocrine functions, thereby avoiding the frequent post-operative panhypopituitarism, so often seen with the standard transcranial approach. Similarly, in the case of an intrasellar chromophobe pituitary adenoma, one has been able to assure himself of a more complete removal of the tumor and its capsule. Finally, when using this approach in hypophysectomy for metastatic breast or prostatic carcinoma or for selected cases of diabetic retinopathy, the surgeon has always been confident of a total removal of the pituitary gland, since it is under direct magnified vision. It should be noted, however, that in cases of large and extensive pituitary tumors, that significantly extend above the sella, with possible optic nerve and chiasm compression, we have preferred to use the more traditional transcranial approach. Hardy, however, using intraoperative fluoroscopy, has successfully removed tumors of this size transsphenoidally.

Despite the several obvious advantages of the transnasal-transsphenoidal approach, this technique does possess one major disadvantage and a source for potential serious difficulties. This relates to the risks of infection and meningitis when approaching the pituitary gland through the partially contaminated transnasal operative field. In addition, there are subsequent hazards for development of CSF infection should there occur postoperative CSF leakage or rhinorrhea. With intra-operative and, particularly, post-operative antibiotics, septic complications do not seem to be any greater than when using the traditional transcranial route. Similarly, following initial development and refinement of operative techniques, the problem of CSF rhinorrhea has also been minimal, and is not now that frequent. Hardy's results[1] seem to paint a similar picture. Several minor problems should also be mentioned. These include a slight change in the quality and resonance of voice during the post-operative period which is usually only temporary. Similarly, there is a short period of post-operative rhinitis related to the operative manipulation of the nasal mucosa. We have also had the impression that the frequency of mild diabetes insipidus is also slightly greater, possibly related to a greater manipulation of the pituitary stalk prior to its division.

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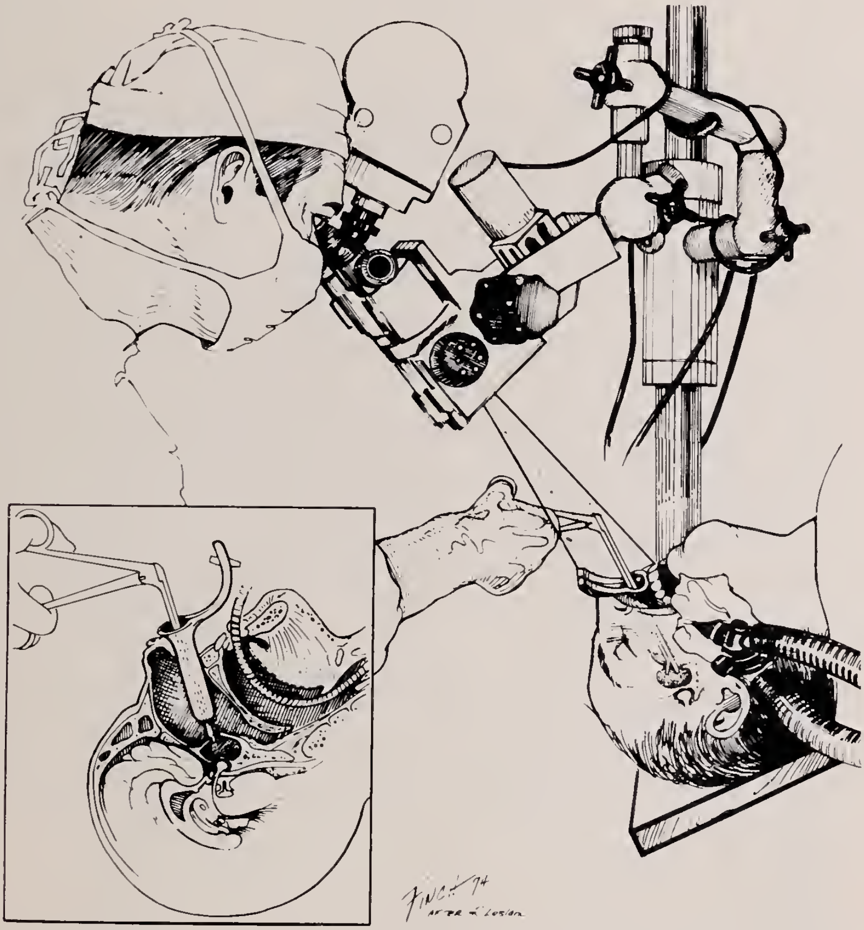
Summary

The use of the operating microscope with its inherent excellent illumination and magnification has allowed rebirth of an old approach to the sella and pituitary gland. This technique utilizes the transnasal-transsphenoidal route (Figure) which possesses several advantages over the traditional transcranial avenue. Currently, we prefer this approach when dealing with a pituitary tumor that is strictly intrasellar, which is a common situation in an endocrinologically active pituitary tumor such as in acromegaly and occasionally with a chromophobe adenoma. On a number of occasions in the former situation, we have been able to selectively excise a small eosinophilic adenoma and at the same time preserve a normal pituitary gland and its endocrine functions. To date, with this approach, we have not attempted removal of larger pituitary tumors with suprasellar extension.



Figure—Operative approach for transnasal-transsphenoidal pituitary surgery utilizing the operating microscope.

Figure (inset)—excising the anterior wall of the sphenoid sinus with the subnasal speculum in place following excision of the nasal septum and vomer.

Similarly, in selected cases of metastatic breast or prostatic carcinoma we have used this technique to carry out a hypophysectomy for further endocrine palliative treatment. In addition, selected cases of diabetic retinopathy might also be treated in this fashion. This would certainly seem to be an ideal approach when confronted with these latter situations, since the procedure allows a total removal of the pituitary gland with a minimum of morbidity.

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Differential Sacral Rhizotomy

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SHELLEY CHOU, M.D.‡

We have recently refined the technique of differential sacral rhizotomy[1,2] for the treatment of neurogenic bladder dysfunction, particularly symptoms of frequency, urgency, and incontinence. These symptoms are due to hyperactivity of the detrusor muscle as determined by air cystometry. Percutaneous selective sacral nerve blocks are used preoperatively to determine whether the operative procedure could be of value in relieving the symptoms.

The surgical procedure is performed under local anesthesia so that air cystometry can be carried out during the operation and the patient can be simultaneously questioned as to the sensation of bladder distension or urge to void. Using the operating microscope, the individual fascicles of the selected sacral roots are in turn stimulated and anesthetized to identify fibers which innervate the bladder only. These fibers are then sectioned, leaving the remainder of the nerve intact. We are thus able to restore more physiologic voiding for the patient by preserving the detrusor reflex and sphincter function but at the same time increasing bladder capacity.

We have performed this procedure in 13 multiple sclerosis patients. There has been initial good relief of symptoms in eight patients with a follow-up of one to three years. Failures have been related to persistent or recurrent detrusor hyperreflexia probably because the initial rhizotomy was not extensive enough. The procedure is designed so that it can be repeated in this situation which we have done in one instance. There has been no morbidity or mortality related to the procedure.

Although this series included only multiple sclerosis patients, the procedure should be equally applicable to patients with detrusor hyperreflexia from other causes. Traumatic paraplegic patients frequently suffer from this urinary problem.

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Scan Conference

Chest Pain

A 25-YEAR-OLD male developed sudden onset of chest pain with dyspnea. The symptoms developed approximately three weeks after he had been hospitalized and confined to bed for a subarachnoid hemorrhage secondary to a bleeding intracerebral aneurysm. The patient was afebrile. A chest film (Figure 1) and lung scan (Figure 2) were obtained shortly after the onset of symptoms. What diagnostic possibilities can be entertained based on these findings? (A) spontaneous pneumothorax, (B) pneumonia, (C) atelectasis, (D) pulmonary emboli. What is your diagnosis? (See next page).

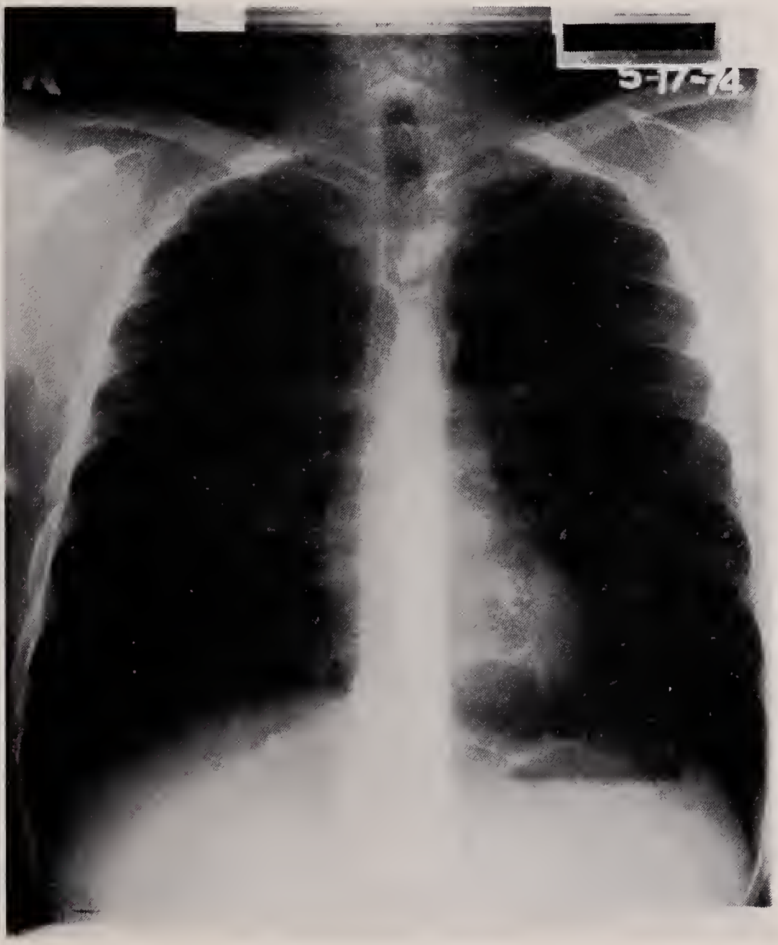

Fig. 1—Normal chest Xray.

Discussion

The patient's chest Xray was normal and ruled out the possibility of pneumothorax, pneumonia or atelectasis. The lung scan (Figure 2) showed multiple perfusion defects occurring in both lungs. There is almost total absence of perfusion in the right lung with only a small segment of the right upper lobe remaining perfused. Multiple marginal defects are noted on the left side. The finding of these multiple defects on the lung scan in the presence of a normal chest Xray is highly suggestive for multiple pulmonary emboli. Another possibility which

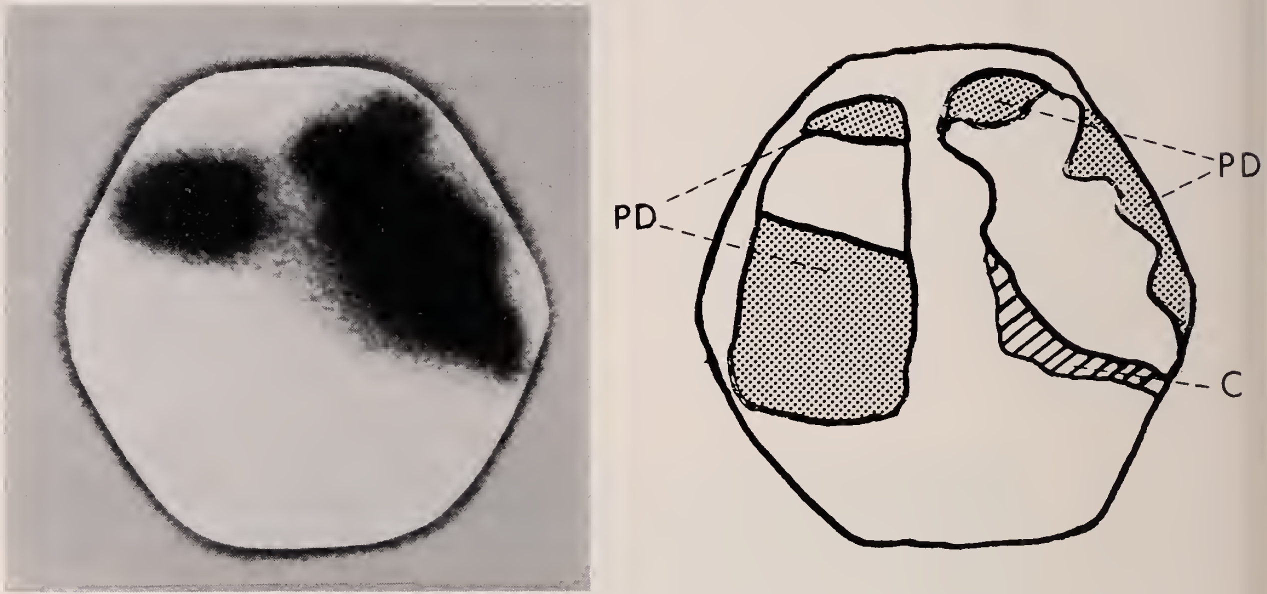

Fig. 2—(Left) Anterior view of lung scan demonstrating multiple perfusion defects in both lungs with almost total absence of perfusion in the right lung. (Right) Outline drawing of lung scan. Shaded areas labeled PD represent areas which are not being perfused because of multiple pulmonary emboli. Area labeled C represents the normal defect caused by the cardiac configuration.

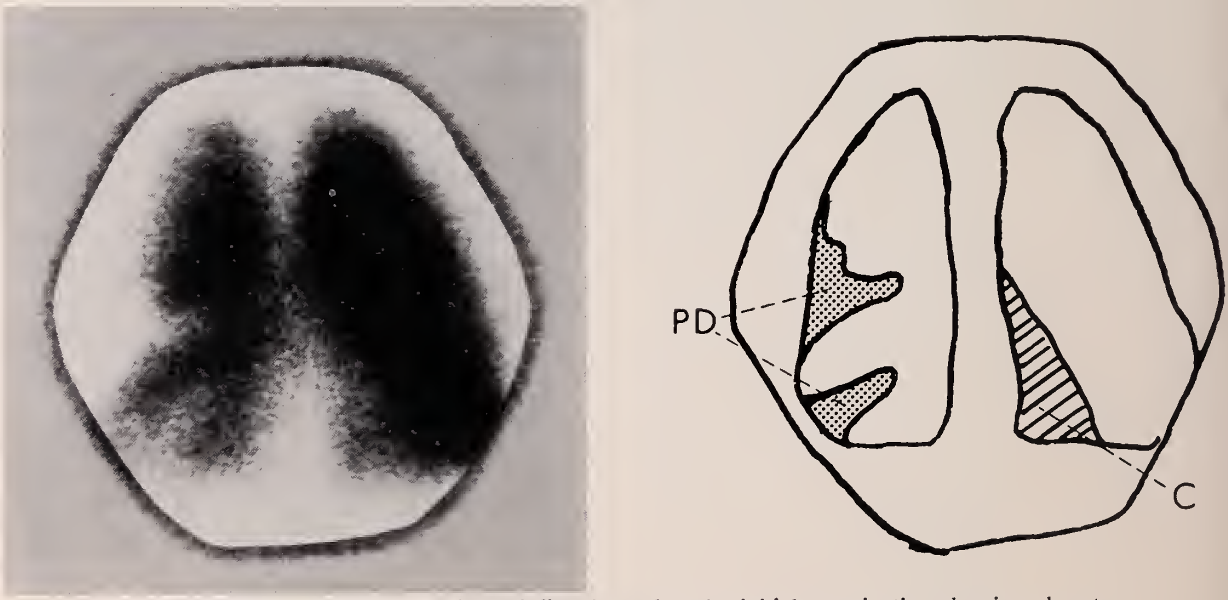

Fig. 3—(Left) Lung scan performed five days after the initial examination showing almost complete re-perfusion of both lungs. (Right) PD represents areas of residual perfusion defect with the lungs being almost normally perfused. Area C represents space occupied by the heart.

could cause defects on the scan without being readily detected by chest Xray would be chronic obstructive lung disease. This problem is encountered more frequently in the older age group and when this is considered to be a diagnostic problem an additional Nuclear Medicine procedure that may be helpful is a lung scan performed with 133-Xenon. This is helpful in detecting areas of obstructive lung disease which may not be clearly separable from pulmonary emboli with the routine perfusion lung scan. Figure 3 shows the anterior view of the lung scan carried out five days later. In this time interval, during which the patient received anticoagulant therapy, there has been a remarkable change in the appearance of the scan. The large areas of absent perfusion are now almost normal. Only a few small irregular areas of residual defects remain within the right mid and lower lung fields. The changing pattern of defects is a characteristic of pulmonary emboli and this is not a pattern one would expect in the presence of obstructive lung disease.

Lung scanning can be very helpful and informative in the evaluation of the patient with chest pain and dyspnea. The intelligent use of a lung scan demands that interpretation be made in association with a concurrent chest Xray. Utilizing these two modalities one can arrive at a specific diagnosis in a large proportion of cases. Lung scanning is a sensitive test for pulmonary embolism. If the scan is normal, this greatly decreases the probability that pulmonary emboli are present. While pulmonary arteriography provides a specific definition of an embolus, its use is declining except in those cases where indicated for pre-operative localization of an embolus.

Marvin E. Goldberg, M.D.*
University of Minnesota

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*Associate Professor of Radiology, University of Minnesota Medical School, Minneapolis.

Continuing Medical Education

More than one hundred (100) Minnesota Internists have expressed interest in a course designed specifically around the voluntary recertification examination content as defined by the American College of Physicians. Accordingly the University of Minnesota Medical School, Department of Medicine, together with its Section on Primary Care and the Department of Medicine, St. Paul-Ramsey Hospital, has announced two refresher courses in response to this interest:

The first runs serially from Thursday, June 20 through September 12, Evenings except for July 4th. The second, a four and a half day concentrated course, will be held Tuesday, October 1 through Saturday October 5. Registration information may be secured by calling the Office of Continuing Medical Education, University may be secured by calling the Office of Continuing Medical Education, University of Minnesota (612) 373-8089 or 8012, or by mail, Box 293, the Medical School, Minneapolis 55455.

Authority and Accountability in Rural Health Care Planning

"Joint Powers" for Rural Health Care Development

STEPHEN NYE BARTON, M.D., M.A.P.A.;* TIMOTHY C. JEFFERY M.A.P.A.†
and JOHN B. O'LEARY, M.D.‡

Although the communities grasped responsibility for health care planning, all medical accountability remains with the physicians who practice in the traditional fee for service relationship with their patients while at the same time encouraging patients to obtain prompt and comprehensive care for illness and proper physical activity and diet to maintain health. The role of research is seen as a feedback loop to provide information on the effect of health care planning and health care delivery on the citizenry served by a given health care system.

RURAL AREAS HAVE suffered a shortage of medical manpower of increasing magnitude.[1,2] The A. K. Rice Institute of the United States and the Tavistock Institute of Human Relations in London each conduct conferences wherein members can experience and thereby understand the perils of abdicating personal responsibility for supporting or confronting leadership.[3] Rural citizens in southwestern Minnesota have experienced the results of abdicating responsibility for creating effective health care systems. By seeing health care as embodied in the physician rather than in a system, some small rural communities have effectively abdicated responsibility for improving "health" and have instead engaged in fruitless attempts to secure physicians.[4] The small towns have not given up easily. But at a time when the increasing complexity of health care resources has required area-wide approaches, communities that have been historically competitive have found it difficult to work cooperatively in improving health services. Thus, the fragmentation of area-wide efforts has resulted in a further abdication of responsibility by preventing effective work on the task of improving health care delivery. Residents of rural communities (members of large groups) have colluded to avoid the responsibility of working cooperatively.

Regionalism

Regional approaches to health care planning have been initiated but have not always been successful in providing effective consumer representation. The Comprehensive Health Plannin
and Public Health Services Amendments of 196
(Public Law 89-749) section 314A and B facilitated the formation of the Minnesota Comprehensive Health Planning Agency and regional comprehensive planning boards within the State o
Minnesota. The comprehensive health plannin
region of southwestern Minnesota consists o
eighteen counties which is sufficiently large fo
regional planning, yet so large that representatives
on the regional board from small towns and townships live at distances from one another tha
effectively diminish their opportunity to interact
Further, one of the basic problems of regiona
health planning boards is that the consumer i
frequently overwhelmed by providers who ar
already deeply involved at the decision makin
level of the health delivery system.[5,6]

The Minnesota Human Services Act of 197
is permissive legislation for use by county board
of commissioners and health, corrections, welfare
and mental health agencies wanting to coordinat
or integrate the planning, budgeting, and programming of human services. One of the prerequisite
for the formation of a human services board i
that the board represent at least 50,000 population. Thus, in many rural areas this requires tha
several counties cooperate. Yet, when the dynamic commercial boundaries of small communities are studied, potential service areas and traffi
flow patterns define natural area-wide cooperativ
planning boundaries which do not necessarily coincide with county boundaries.[7,8]

Although regional approaches to health car
planning must continue, small villages and town
must join together if they are to have a voice i
the larger regional health planning process.

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*Health Care Development Director, Southwest Minnesota Health Care Enterprise, Inc.

†Assistant City Manager, Richfield, Minnesota.

‡Associate Professor, Department of Family Practice, University of Minnesota, Minneapolis.

Flexibility

In the year 1971-72, six communities in rural southwestern Minnesota joined together through the formation of a nonprofit corporation to investigate ways of cooperatively planning for health care. The nonprofit corporation, Southwest Minnesota Health Care Enterprise Inc., consisted of two directors from each of the six communities (Wabasso, Wanda, Revere, Storden, Jeffers, and Lamberton). The directors are elected each year at an announced meeting of the corporation. The initial work was initiated with a small grant from Northlands Regional Medical Program. The flexibility of a nonprofit corporation facilitated the formulation of a total health care concept emphasizing ambulatory care, transportation, health education, and preventive medicine programs.[9] Three physicians were recruited and a physician from the University of Minnesota visits the ambulatory care center twice monthly. The work of the nonprofit corporation stemmed from the assumption that "the quantity of medical services that the population wants to consume may be different from the quantity of medical services the medical profession feels, in its opinion, the population members need and ought to consume."[10] It was recognized that "above all, multiple communities, in a logical service area, will need to plan together to develop *health care systems* on an enlarged area basis to attract appropriate health manpower."[11]

Need for Accountability

The nonprofit corporation represents the communities only indirectly. Each director is not appointed through a political process involving governmental accountability. The lines of authority were blurred by the lack of official governmental power to act on behalf of the citizenry. Fortunately, Minnesota statute section 471.59 authorizes the joint exercise by two or more public agencies of any power common to them. This is done through the formation of a "joint powers agreement" between governmental units seeking a cooperative area-wide approach in the solution of problems.

In January, 1974, ten cities and twelve townships in southwestern Minnesota entered into a joint powers agreement to form Southwest Minnesota Health Services Board. The general purpose of the agreement was to provide an organization to which the parties would jointly and cooperatively coordinate the delivery of health services both publicly and privately in the territory of the parties. Each governmental unit participating in the agreement was entitled to appoint two directors. Thus, official delegation of authority was executed.

The powers and duties of the board are as follows:

1. It may employ a person to act as an executive director of the board.
2. It may make such contracts as the board deems necessary and advisable to make any power effective to be exercised by the board pursuant to the provisions of this Agreement.
3. It may employ such other persons as it may deem necessary to accomplish its powers and responsibilities.
4. It may conduct research and investigations regarding existing and possible future health care services, facilities and programs and may develop a proposed plan for the delivery of health care services.
5. It may apply for and receive financial support from other organizations, governmental units, agencies, or foundations in order to accomplish its purposes and may enter into agreements necessary to obtain such financing.
6. It may prepare a plan for the delivery of health care services and shall report any such plan back to the parties for further action and direction.
7. It may enter into any contracts deemed necessary by the board to carry out its powers and duties subject to the provisions of the Agreement.
8. It shall make a financial accounting and report to the parties at least once a year and its books and records shall be available for and open to an examination by the parties at all times.
9. It may exercise any other power necessary to the implementation of its powers and duties under the provisions of this Agreement.

Community Medicine Specialist

The British National Health Service reorganization of 1974 envisions the creation of specialists in community medicine. Their concern will be with assessing need for health services, evaluating the effectiveness of existing services and planning the best use of health resources.[22] Unfortunately, small rural communities and townships with less than 1,000 population can not afford full time professional health care planners. Yet, state-wide and regional commissions frequently fail to be responsive to consumer demands. Thus, the cooperative approach outlined emphasizes the need for the citizenry to become specialists in community medicine.

The Feedback Loop

"One of the greatest deficits which hampers both the state and area-wide health planning councils as well as all other planning bodies is the lack of a data base . . ."[13] Just as an inadequate data base fosters poor patient care, the lack of adequate information about a population's health seeking behavior, health status, health resources, demographic characteristics, and other variables prevents the citizen from becoming an effective community medicine planner. Planning must be based on objective data to assure accountability. It follows that data collection must conform to the methodology of research in the behavioral and social sciences.

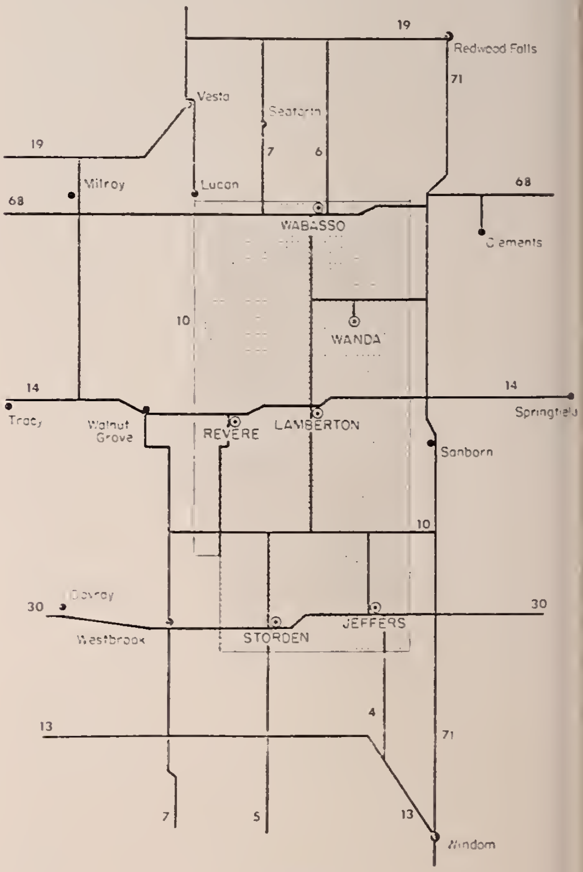
When planning is based on myth it can fail. Like the natives in the South Pacific during World War II who saw the airplanes landing with cargo, many small towns developed a cargo cult. Just as the New Guinea natives built replicas of landing fields in the jungle to attract cargo, little towns build clinics but can find no doctor. Unraveling the complexities of rural health planning requires objective and accurate data. A community of less than 1,000 persons rarely has the resources for this type of data gathering. For this reason. rural health care development requires a joint effort by professionals and consumers in the collection and use of information. An inter-institutional, inter-agency and inter-community approach is an alternative to isolated community approaches that have been unfruitful.

In this study, the nonprofit corporation functioning as an intergroup representing six communities, aggressively obtained information describing the area population characteristics: age distribution, economic patterns. housing, selected mortality statistics, traffic flow patterns, and mental health indexes. Further, all regional and area health resources were identified and characterized. It was recognized through these efforts that "rural communities are not mutually exclusive and exhaustive territories and that interdependence with larger political, economic, and urban units is ever increasing."[14]

Facilitated by a grant from Northlands Regional Medical Program the department of Family Practice and Community Health at the University of Minnesota Health Sciences Center assisted the rural communities by initiating a longitudinal health status and health seeking behavior survey in 1972. Initial studies in the six community research area (Figure) based on a random stratified sample c the population revealed that improving denta health was a high priority task.[15] A dentist wa recruited to implement a dental health educatio program. Further, the survey of health seekin behavior revealed an episodic rather than a maintenance pattern of utilization. There also was significant delay by the elderly in seeking healt care. Herein rested the data base for communit health care planning and the creation of an ambulatory health care delivery system utilizing regional resources and a comprehensive approach.

Thus, research provides a feedback loop tha facilitates planning based on objective data rathe than myths.

The success of the organizational model described here does not rest in the success the communities had in the procurement of physicians The physicians could leave. The clinics coul close. The needs of the area will change wit time. Health education could become the highes priority. Transportation could yield alternativ approaches. Regionalism could make certain services redundant. The importance of this demon-



Figure

stration model lies in its ability to facilitate the grasping of responsibility on an area-wide basis for the improvement of "health" rather than abdicating authority or engaging in fruitless efforts based on myths. The organizational model outlined is by its very nature dynamic rather static and thereby is not locked into traditional fragmented precedents frozen in chaos.

Summary

If the maldistribution of physicians continues rural areas will suffer a medical manpower shortage of increasing magnitude. To facilitate the location of physicians in rural communities requires the provision of a rural health care system utilizing an area-wide planning approach. The lines of authority and accountability were clarified when ten cities and twelve townships in southwestern Minnesota entered into a "joint powers agreement" for the purpose of rural health care development. A nonprofit corporation consisting of representatives from six rural communities from southwestern Minnesota provided the flexibility necessary to initiate an ambulatory health care system and thereby facilitate the recruitment of three physicians.

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It's the Law

$351,000 Verdict Against Physician for Failure to Disclose a Condition of Asbestosis

A 56-year-old machinist who worked in an asbestos plant was examined by the company physician in 1962, 1965 and 1968. The physician found advancing signs of asbestosis but failed to advise the patient of this fact, to refer the patient to a chest specialist, and failed to recommend a change in working conditions.

The patient brought suit against the physician claiming permanent and total disability due to lung damage and claimed as well, a substantial reduction in life expectancy because of pulmonary asbestosis.

The court awarded $351,000 verdict to the patient.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Vella vs. Weise (California Superior Court, Conta-Costa Co.) Document #116083 November 1, 1973, The Citation.

Book Reviews

PARENTS' GUIDE TO ALLERGY IN CHILDREN—Claude A. Frazier, M.D., 1973 Doubleday and Co., New York, New York, 338 pages—$7.95.

Claude Frazier has written a book which provides an excellent guide for parents who have an allergic child. It makes no attempt to either help diagnose or treat. As stated by Claude Frazier, these problems are best handled by a qualified physician. Allergy is an individualistic disease and needs specialized diagnosis, treatment and management.

This book covers practically all of the common aspects of allergy. It begins with an excellent introduction in the form of a "Panoramic View." Following this such subjects as the Allergist, diagnosis and desensitization are nicely explained for the layman. There are chapters on inhalants, food allergy, drugs and other of the more common allergens. The chapter on food allergy includes an interesting Botanical list of food families. The subject of moving to a different climate is discussed as are immunizations and surgery in the allergic child. The complex question of emotions and their role in the allergic child is covered in a well presented chapter. Each chapter has a nice summary entitled "Things to Remember."

Parents' Guide to Allergy in Children is an excellent book. It not only contains a wealth of factual material but is also well written. Considering one child out of every four to five suffers from a major allergy, this book should be of great benefit to many of these parents. It is highly recommended.

Willard C. Peterson, M.D.
Minneapolis, Minnesota

TECHNOLOGY AND INTERPRETATION OF NUCLEAR MEDICINE PROCEDURES—Sodee-Early. C. V. Mosby, $22.90.

This book is intended as a manual of Nuclear Medical procedures. It is based on information presented in the earlier "Textbook of Nuclear Medicine Technology." This manual is divided into two parts—the first is a laboratory guide to nuclear instrumentation, radiochemistry and health physics. The second part contains information on the physiologic basis and interpretation of clinical Nuclear procedures. In addition to the named authors, there are eleven individuals who contributed materials for this manual.

For the most part, the material as presented is factual. There are however errors related to determinations of resolving time and of counting statistics. In addition, the inclusion of materials such as Chapter 14 on efficiency is to be questioned.

It appears that this manual will be of value for those who participate in training sessions held at the authors' institution. Beyond this, it appears doubtful that the materials will be generally applicable.

Merle K. Loken, M.D., Ph.D.
University of Minnesota

PSYCHOSOCIAL ASPECTS OF CYSTIC FIBROSIS: A MODEL FOR CHRONIC LUNG DISEASE. Edited by Paul R. Patterson, Carolyn R. Denning, and Austin H. Kutscher. Published by The Foundation of Thanatology, Distributed by Columbia University Press. New York and London, 1973.

This multi-authored book is the product of a symposium on the psychological aspects of the chronic and potentially lethal disease, cystic fibrosis. The book reflects the experiences and interpretations of many physicians around the United States who are caring for these children. The patients under their care range from severely affected children with a limited life expectancy to children who seem to be surviving as healthy as their birth cohorts because of prophylactic care. The psychological stresses of the mixture of complications present in these patients, the constant knowledge that death will occur from these complications, and the distant hope for a cure to which all the families cling provide a background for a most interesting reading for physicians, psychologists, social workers, and nurses dealing with a chronically ill child who is expected to die from his disease.

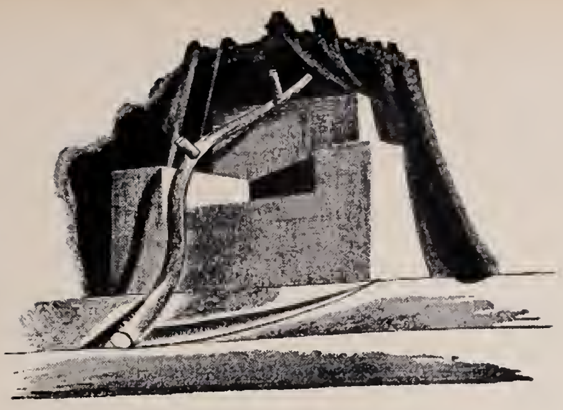
Warren J. Warwick, M.D.
Department of Pediatrics
University of Minnesota

MEDICARE AND SOCIAL SECURITY by Bruce Biossat. Doubleday and Company, Inc., 114 pages. Price: $1.95.

For anyone approaching retirement age, this paperback book provides all of the answers that might concern one in making plans for the amount of money that will be forthcoming.

Table of Contents and the Index are adequate to direct one to the interest that may be at hand.

Carl O. Rice, M.D., Ph.D.
Editor Emeritus



In Memoriam

RICHARD R. TEETER. M.D.

Dr. Richard A. Teeter, 51, director of in-patient adult psychiatry at St. Paul Ramsey Hospital, died May 13. He had been a member of the St. Paul Ramsey Hospital medical staff since 1965 when he assumed the post of chief of psychiatry, a position he held until 1971. Dr. Teeter was also coordinator of medical education for the Psychiatry Department of the Hospital.

His medical degree was obtained at the University of Pennsylvania. Dr. Teeter is a member of the Ramsey County Medical Society, the American Medical Association and the Minnesota State Medical Association.

He is survived by his wife, Ruth, and a son, Dan, and a daughter, May.

DONALD E. DILLE. M.D.

Dr. Donald Dille, 52, Litchfield physician, died March 21, in a car mishap. He had practiced medicine in Litchfield for 28 years.

A native of Dassel, Dr. Dille graduated from the University of Minnesota Medical School. He was a past president of the Meeker County Historical Society, a member of the Litchfield School Board, American Medical Association, the Mid-Minnesota Medical Society, and the Minnesota State Medical Association.

Dr. Dille is survived by his wife, Bonnie, and seven children.

DOUGLAS M. GARROW, M.D.

Dr. Douglas M. Garrow, 51, St. Paul physician, died May 14. He had practiced medicine in St. Paul for 40 years.

A graduate of the University of Minnesota Medical School, Dr. Garrow was a member of the American Medical Association and the Ramsey County Medical Society and a Life member of the Minnesota State Medical Association.

Dr. Garrow is survived by his wife, Marion, and daughters, Jean and Betti.

CARL C. CHATTERTON, M.D.

Dr. Carl C. Chatterton, 88, orthopedic surgeon and former chief of staff at Gillette Children's Hospital for 35 years, died May 18. He had received the Cosmopolitan International District Service Medal in 1937 for his work with crippled children. His medical education was obtained at Northwestern University Medical School.

He was the first resident in orthopedics of Dr. Arthur Gillette, the physician instrumental in founding the hospital for children which is named for him. Dr. Chatterton was a member of the American Academy of Orthopaedic Surgeons, the Orthopaedic Association of the American College of Surgeons, the American Medical Association and the Ramsey County Medical Society, and a 50 Club and Life Member of the Minnesota State Medical Association. During his medical career, Dr. Chatterton was a member of the staffs of most St. Paul hospitals and a clinical professor of the University of Minnesota.

He is survived by his widow, Laura, son William and a daughter, Laura.

HORATIO B. SWEETSER, JR., M.D.

Dr. Horatio B. Sweetser, 76, former chief of staff at St. Mary's Hospital and past president of the Minnesota State Medical Association, died May 5. He was also founder and medical director of St. Mary's Hospital's Extended Care Center.

A graduate of Harvard Medical School, Dr. Sweetser was on the Board of Directors of the Minnesota Division of the American Cancer Society and was a member of the American Medical Association, the Minneapolis Academy of Medicine and a 50 Club and Life Member of the Minnesota State Medical Association. He had a private practice in Minneapolis and was clinical associate professor of medicine at the University of Minnesota until 1966.

Dr. Sweetser is survived by his wife, Mary, and daughter, Margaret.

DEAN M. VEIRS, M.D.

Dr. Dean M. Veirs 89, Hastings physician for 40 years, died April 9. He was also a former staff physician at the Hastings State Hospital, and on the staffs of St. Paul Midway Hospital for 30 years and Bethesda and St. Luke's Hospitals.

Dr. Veirs was a member of the American Medical Association, the American Academy of General Practice and the Ramsey County Medical Society, and a 50 Club and Life Member of the Minnesota State Medical Association.

He is survived by his daughter, Bettie Jayne.

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Replies to advertisements with key numbers should be mailed in care of Minnesota Medicine, 375 Jackson, St. Paul, Minn. 55101.

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(Continued on page 597)

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(Continued from page 596)

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Meetings

North Dakota Internal Medicine Specialists

Specialists in internal medicine and related fields will hold a one-day scientific meeting on September 7, 1974, at the Holiday Inn in Bismarck, ND.

The North Dakota Regional Meeting of the American College of Physicians (ACP) is designed to bring physicians up-to-date on late developments in the field of internal medicine. INFO: P. Roy Gregware, M.D., 1239 W. Highland Acres Road, Bismarck, ND 58501.

Wisconsin Internal Medicine Specialists

Specialists in internal medicine and related medical fields will hold a two-day scientific meeting on September 13-14, 1974, at the Telemark Lodge in Cable, WI.

The Wisconsin Regional Meeting of the American College of Physicians (ACP) is designed to bring physicians up-to-date on late developments in the field of internal medicine. INFO: George E. Magnin, M.D., 630 South Central Avenue, Marshfield, WI 54449.

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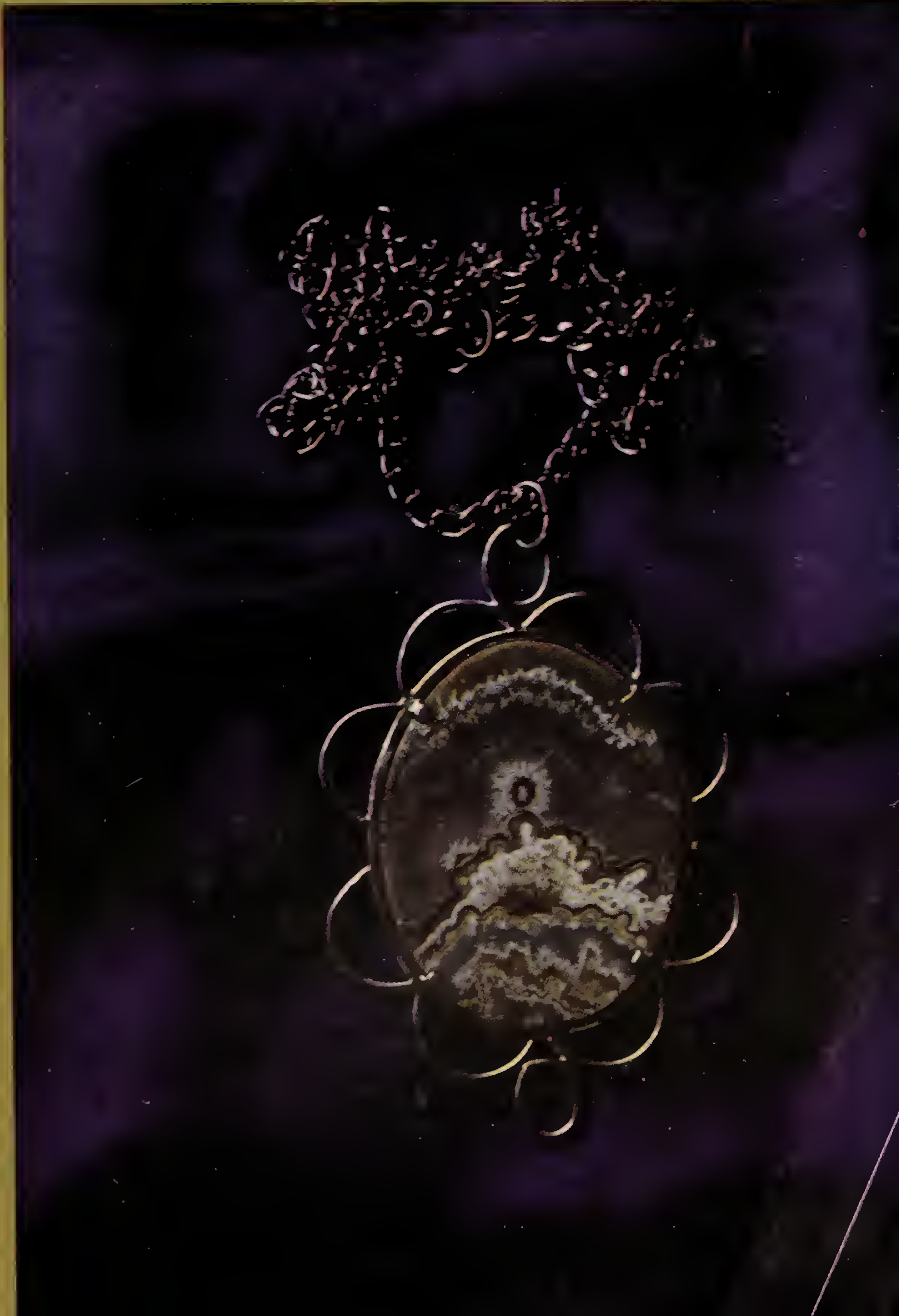
Aging

Special Issue

AUGUST 1974



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Ferdinand A. Zinter, M.D.

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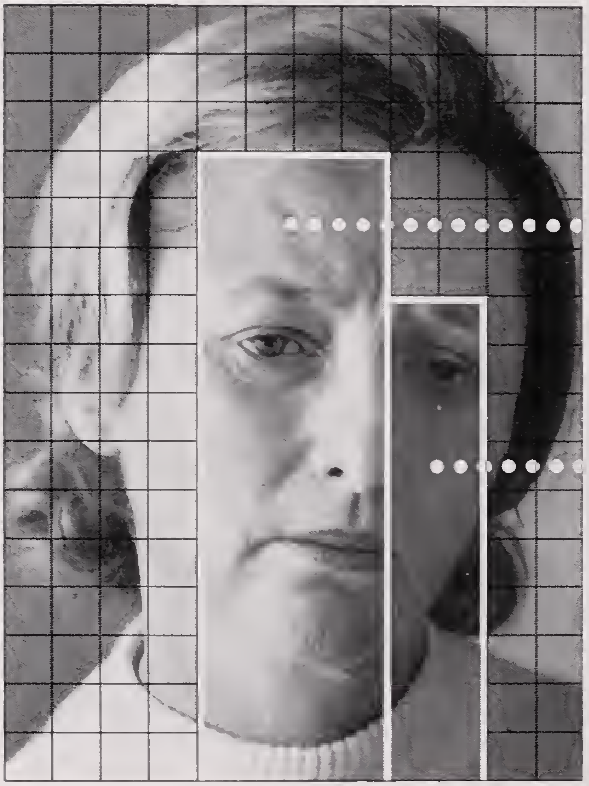
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Associated depressive symptoms

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and/or severity of grand mal seizure
require increased dosage of standar
convulsant medication; abrupt with
may be associated with temporary i
crease in frequency and/or severity
seizures. Advise against simultaneo
gestion of alcohol and other CNS de
sants. Withdrawal symptoms (simil
those with barbiturates and alcohol)
occurred following abrupt disconti
(convulsions, tremor, abdominal an
cle cramps, vomiting and sweating)
addiction-prone individuals under c

respond to one

ccording to her major
toms, she is a psychoneu-
patient with severe
ety. But according to the
ription she gives of her
ngs, part of the problem
sound like depression.
is because her problem,
ugh primarily one of ex-
ve anxiety, is often accom-
ed by depressive symptom-
gy. Valium (diazepam)
rovide relief for both—as
xcessive anxiety is re-
d, the depressive symp-
associated with it are also
relieved.
There are other advan-
in using Valium for the
agement of psychoneu-
anxiety with secondary
essive symptoms: the
hotherapeutic effect of
m is pronounced and
. This means that im-
ement is usually apparent
e patient within a few
rather than in a week or
two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

For further information on this subject, the following references are provided:

1. Henry BW, *et al: Dis Nerv Syst 30*:675-679, Oct 1969.
2. Hollister LE, *et al: Arch Gen Psychiatry 24*:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics 11*:438-441, Sept-Oct 1970.

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with associated
depressive symptoms

illance because of their predisposi-
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ancy, lactation or women of child-
ng age, weigh potential benefit
st possible hazard.

utions: If combined with other psy-
opics or anticonvulsants, consider
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d; drugs such as phenothiazines,
tics, barbiturates, MAO inhibitors
ther antidepressants may potentiate
tion. Usual precautions indicated in
nts severely depressed, or with latent
ssion, or with suicidal tendencies.
Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

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President's Letter

Minnesota Was There

THE MEETING OF the American Medical Assoiation have always seemed something to be voided. Reports of the number of doctors in ttendance were unbelievable. But one of the uties of the President of the State Association is ttendance at the Annual Session, so I went to hicago in June for the 123rd Annual Meeting f the AMA. As the week progressed, my doubts vere replaced by admiration for the organization f the meeting. There was practically no crowdng or confusion, despite the attendance of nearly ight thousand physicians. The scientific sessions t McCormick Place were diversified and of high aliber. The committee and House of Delegates neetings were generally well ordered and producive. And importantly for us, amidst all this ctivity, the participation of Minnesota physicians vas significant and their leadership effective.

Dr. Robert Kelly had been nominated by the Board of Trustees of the AMA to a seat on the Medical Services Committee. This committee, dealing with socio-economic affairs, is one of the nost important permanent committees. It was eartwarming to see the Minnesota delegates as vell as those from the North Central States rally round Dr. Kelly's candidacy: twist arms, persuade other delegations, and generally make his position known. It was a good excuse as well to visit the hospitality suites of other states, drop off campaign literature, put in a few words for our candidate, and listen to their pitches for their local favorites. Dr. Kelly conducted himself well and was successful in his campaign.

Dr. Charles Verheyden, an intern-resident candidate from the Mayo Clinic was elected to a seat on the Council on Medical Education. He was jointly sponsored by Minnesota and Texas.

Dr. George Martin had been appointed Chairman of Reference Committee A which is probably the most important of all the reference committees. This appointment was a high tribute to his ability since Reference Committee A was scheduled to receive testimony on PSRO. Consideration of this issue began at 1 PM and concluded at 5:30 PM after sixty-four physicians had spoken. Speeches ranged from studied, restrained logic to flowery, emotional eloquence. Supporters of repeal came generally from the South and some of the smaller states. Others favored compliance, but with amendment of the law. Many states had operational review programs and felt it important that medicine have input and retain control, rights that we abdicate with support of repeal.

Dr. Martin's committee's moderate stand on the problem, surprisingly, was accepted without debate by the House of Delegates. Dr. Martin received a standing ovation for the committee's masterful handling of a difficult decision.

Mr. Harold Brunn, our premier Executive Secretary, was inducted as President of the American Association of Medical Executives. It was my privilege to introduce him at the luncheon ceremoney. There were about three hundred in attendance, and it was obvious that Harold is very popular and much admired among his peers.

The Minnesota delegation had also introduced a resolution asking the AMA to seek an appropriate amendment to the HMO Act of 1973 which would require any employer offering only HMO membership to his employees to also offer an alternative choice of health benefit through a standard policy of health and accident indemnity insurance. This resolution was one of the more substantive introduced at the meeting and passed without opposition.

(Continued on page 617)

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Opinion & Dialogue

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Dr. Willard Gobbell
Family Physician
Encino, California

“I may be prejudiced, but
very much in favor of the detail
I meet. Most of them are knowl
able about the drugs they prom
and can be a great help in acqu
ing me with new medication.”

Family Physician's Perception

I think that most general
practitioners in this area feel a
do about the detail man. Over t
years I have gotten to know mo
the men who visit me regularly
they in turn have become awar
my particular interests and the
ture of my practice. They, there
fore, limit their discussion as m
as possible to the areas of inter
to me. Since I usually see the s
representative again in future
visits, it is in his best interest t
supply me with the most hones
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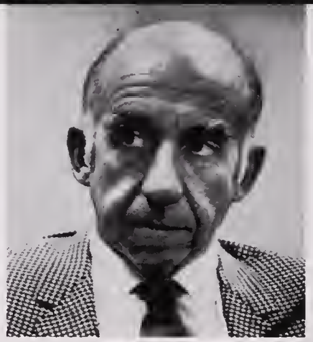

Dr. Jeremiah Stamler
Chairman
Department of Community Health and Preventive Medicine, and Dingman Professor of Cardiology
Northwestern University Medical School

“In the total picture of dea
with health problems in this co
there is a potential for detail m
to play a meaningful role.”

The Positive Influence

My contact with represen
tives and salesmen of the phar
ceutical industry is the type of c
tact that people in a medical ce
research people, and academic
people have and that's in all lik
on a somewhat different level f
that of the practicing physician

Let me touch on how I per
ally perceive the role of the sale
representative. These men rea
large numbers of health professionals. Thus they could be—a
at times actually are—dissemi
tors of useful information. They
could consistently serve a real e
cational function in their ability
discuss their products.

At present they do distrib
printed material, brochures an
pamphlets—some of it scientif
ally sound and therefore truly u
ful—as well as some excellent
produced by the pharmaceutic
industry. When they function i

a Source of Information?

Yes, with certain reservations.
average sales representative
a great fund of information
ut the drug products he is re-
sible for. He is usually able to
ver most questions fully and
ligently. He can also supply
ints of articles that contain a
t deal of information. Here,
exercise some caution. I usu-
accept most of the statements
opinions that I find in the
rs and studies which come
the larger teaching facilities.
es without saying that a physi-
should also rely on other
ces for his information on
macology.

ning of Sales Representatives

Ideally, a candidate for the
ion as a sales representative
harmaceutical company
ld be a graduate pharmacist
has a questioning mind. I don't
this is possible in every case,
so it becomes the responsibility of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

city they are indeed useful;
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eminate broadly based educa-
l material and serve not just
ushers" of their drugs.

ther Side of the Coin

Obviously, the pharmaceuti-
ompanies are not producing all
naterial as a labor of love—
are in the business of selling
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d sales representative can
a negative influence on the
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ndustry Responsibility

Since the detail man must be
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maceutical company, he
ld be carefully selected and thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.*, the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that information must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

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Aging

Pressing Problems and Emerging Needs

R. A. JENSEN, M.D.*

THE POPULATION EXPLOSION following World War II centering largely in the increased birth rate is currently subsiding. Less appreciated is the steady increase in the number of persons 65 years of age and older which has been occurring since the turn of the century and that segment of the population 85 years and older will steadily increase in the years ahead. In 1960 there were 929,000 persons 85 years plus. The Bureau of the Census projects 1,929,000 by the year 2000.[1]

How many older Americans are there? The following figures from the United States Department of Health, Education and Welfare are significant:

1. In 1970, one in every 10 persons in the U.S. was 65+—20.1 million men and women.

2. This number is about the same as the total population of the 22 smallest states.

3. In this century, the *percentage* of the U.S. population aged 65+ more than doubled (from 4.1% in 1900 to 9.9% in 1970), while the number increased more than sixfold (from three million to 20 million).

4. At present death rates, the older population is expected to increase 46% to 29 million by 2000. If the present very low birth rate continues, these 29 million will be 10.6% of the total population of 271.1 million.[2]

Even more significant is the following: "In this century, the 65+ population has grown faster than the total population but the 75+ has grown even faster. At the turn of the century, every 25th American was 65+; by 1990, at least every 10th American will be 65+. At the turn of the century, of the eight million who were 65+, 30% or only 900,000 were 75+; by 1990, there will be 27 million aged 65+ and 40% or more than 10 million will be 75+. In other words, by 1990 the 65 to 74 age group will be 7½ times as large as in 1900 but the 75+ group will be 11½ times as large."[3]

Allowing for deaths in this age group, annual net increase is approximately 225,000 persons.[3]

Minnesota ranks ninth among states with a population of 421,000 of age 65 years+ in 1972 or 11.6% of the total population.[2]

This extraordinary increase in the members of the aging population is a completely new sociological phenomenon which has never occurred in recorded history. With no guidelines from past experience to deal effectively with the many problems which will inevitably arise, close attention is required of all citizens including the physician to assure the aging person proper consideration and care as needed.

It is the purpose of this paper to delineate a few pertinent areas of concern and to emphasize the emerging needs of this group, particularly the need for protective services to those older persons, who, with minimal assistance, would be able to function independently. This in itself would represent a substantial saving in every section of living not only for the older patient but also for everyone of us.

For the medical profession a foremost area of concern is the significant increase in the number of chronic medical problems requiring attention, the cardiovascular disorders, malignancies, degenerative conditions such as arthritis, genitourinary problems, diabetes and the vast array of nutritional disorders. Each one of these categories is likely to be a chronic condition and in most instances multiple. Every chronic medical condition requires not only attention to the immediate problems but also sustained support and care over a prolonged period of time. Essential in many situations is the incorporation and coordination of other supporting services, physical therapy, occupational therapy, social work services, etc., often not available.

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*Emeritus Professor of Psychiatry, University of Minnesota, Minneapolis, Minnesota.

The psychiatric disorders of the aged are dealt with in another paper in this issue.* "A knowledge of symptomatology is not as important as information about the modifiability and the medical, environmental, or emotional changes required. The double play of a quick diagnosis, then disposition to hospital, commitment, nursing home or guardianship is interfered with by such an attitude. It is medieval to think of a psychosis at any age as a problem of competency or confinement, just by virtue of a diagnosis. There are as many kinds of senescent problems as there are people with such problems.[4]

Macmillian states: "The chief manifestations of what is called senile psychosis or senile dementia are not organic; they are an emotional response to unfulfilled basic emotional needs . . . Over and over again we have found that geriatric psychiatric conditions, which used to be regarded as wholly organic and permanent and necessitating hospital admission, are in fact partly organic and partly reactive, and that the reactive symptoms are the more disabling."[5]

If the above be accepted, our standards require change; if such mental illness in older patients is not entirely organic, much could be reversed and prevented.

Another area of concern for the medical profession is the small number of physicians concerned about the total health problems of the older group. This might be accounted for by the oversights of those predicting population trends, and by the sudden awareness of the population explosion in the older age group. There are few places offering training programs in this area. Little attention is accorded the needs of the older group in the medical schools and teaching hospitals.

The first school for gerontology is soon to be established at the University of Southern California made possible by a private grant of two million dollars. This according to John Hubbard, U.S.C. president, "will make it possible to educate professionals who will devote their efforts to solving the problems of the elderly. . . . It is increasingly apparent that there are dramatic shortages of personnel concerned with the problems of aging at a time when the nation's older population is increasing at an unprecedented rate."[6]

Important to the concerns for the aged is the influence of rapid industrialization, the unprecedented migration to the urban and suburban areas of the country, the building of smaller homes and apartment complexes to meet the demands of those living in the new areas, the increased mobility of our population with an estimated 30% always on the move, the expansion of the labor force to include women, many of whom are mothers, and the current unfavorable hiring practices against employing older persons. These and other changes have literally stripped the aged of the responsibilities and functions they possessed in an agrarian society and has left too many unproductive and dependent, generating among many a feeling of uselessness. These profound shifts have forced many into a state of dependency. The median annual income for many is at or lower than that required for adequate living. Approximately 30% live under poverty conditions. Is it any wonder that a significant number of the older group, at times become problems to the community and themselves? Estimates suggest that half a million older persons lack the capacity to manage their personal affairs due to forgetfulness, eccentricities, and confusion.[7] Many are lonely, without friends or family or victims of exploitation, cruelty and neglect. Some become a danger to themselves and to others.

Few among us have not encountered an older person who occasionally may be confused, lost, reckless and irresponsible with his finances, or belligerent and antagonistic when he rejects plans formulated in his best interests. When brought to our attention we face the same dilemma as the rest of the community—to whom to appeal for assistance. To date there is no designated agency or program in any community in Minnesota to expedite the resolution of these difficulties.†

It is a sad commentary that little if anything is done until a crises arises! Under such circumstances alternative courses of action are seldom considered adequately, often to the disadvantage of the individual involved. In too many instances commitment to a state hospital follows. In 1959 the national admission rate to mental hospitals was two and a half times greater for this age group than for younger age groups.[8] Many times an abrupt placement in a nursing home is arranged, but this too has been found unsatisfactory n many instances. A recent book, "As We Are Now," by May Sarton,[9] has this to say: "Nursing homes are the dumping grounds for aged castoffs from every level of society and neither class, education, nor power status can protect an older person from the tyranny of the institution once he gets inside."[10]

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*See page 618.

†1970-73 a demonstration Protective Services Project was established and maintained by the Ebenezer Society of Minneapolis supported by a federal grant. It was discontinued because of lack of financial support from the local community despite a creditable demonstration of need during that period.

A third alternative which at present is not available and has not received serious attention to date is the development and support of a program of protective services for dependent older persons to assure their rights and maximum consideration for their sense of well-being.

The idea of Protective Services for the Older Person was proposed by the National Council on Aging in the early 60's. This organization has conducted conferences emphasizing the need for such service. "Twenty-two states submitted recommendations to the White House Conference on Aging concerning the need to provide protective services for such people. The concern cuts across all economic groups. Not only are public and voluntary welfare and health agencies concerned, but banks, trusts and insurance companies as well are aware of the need for a personalized type of care and supervision that cannot be met by the service they are currently prepared to give."[8]

What are Protective Services? "Those activities undertaken and coordinated by a protective service agency (or program) on behalf of impaired older adults, who are unable or unwilling to act for themselves to secure the help they need to sustain life and/or protect their own interests."[11]

An effective program of protective services requires fulfillment of a threefold function:

1. Assurance that the resources of the individual as well as those of the community will provide the older person with proper care in accordance with need.

2. Safeguarding the individual's rights and his resources.

3. Protecting the individual when his behavior endangers himself and/or others.

Achieving these functions is indeed a complicated process for which there are few guidelines yet established. In addition, the cooperation and integration of all community agencies and resources as well as the expertise of all professional personnel will be required. Admittedly a Herculean task but essential to provide adequately for the needy older person.

In the development of such a program, "there is a need for the real physician—one who is involved with the clinical, social and psychological aspects of the patient, one who is concerned about how his patient's care is organized and one who is willing to follow his patient's care after all else fails."[12] In addition the physician should be willing and able to integrate his skill and expertise with others in the community.

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Yet prodigal of life, the leap he tries,
Low in the dust his groveling honour lies,
Headlong he falls, and on the rugged stone
Distorts his neck, and cracks the collar bone.*

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*John Gay: The Birth of the Squire. 11. 69-72. 1720.

Perceptual and Psychological Changes in Aging

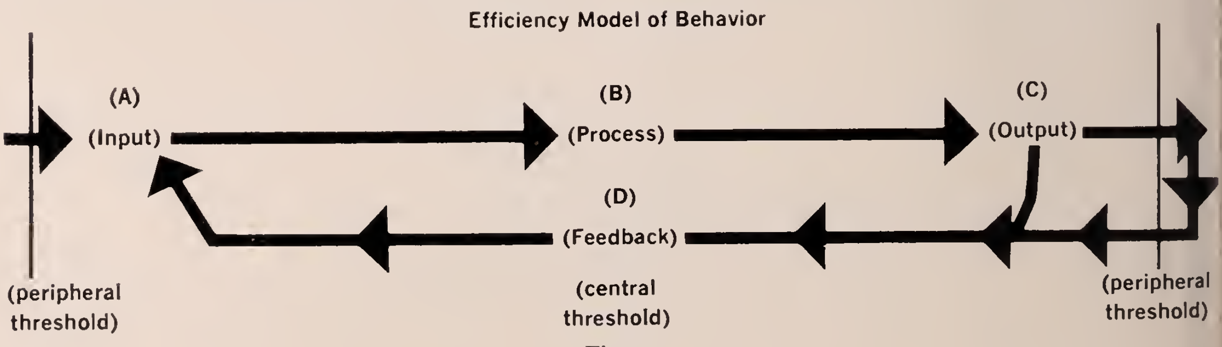
An Efficiency Model*

PETER R. PETH, Ph.D.†

In the news months ago was the story of a Minnesota centenarian who, upon reaching his one hundredth birthday, was approached by a reporter who eagerly inquired, "How does it feel, being one hundred?" "Well," came the deliberate reply, "I can't see or hear, I've lost all my teeth, and I can't remember one day to the next. Now, what was it you wanted to know?!" This anecdote illustrates several important points relevant to this paper and understanding the aging. First, being one hundred years of age implies a special social status, as does simply being "old."[18] Human aging popularly is regarded as a simple matter of the accumulation of birthdays. Secondly, physical changes associated with aging processes, as our centenarian relates, confer upon old age a negative value. Impaired, insolvent, diseased *and aged* persons have almost no social utility, not only in larger society, but often among their age peers. Health care and service providers may have similar attitudes.[15] Increased incidence of physical and emotional problems associated with advancing age support notions of old age as undesirable, pejorative, and synonymous with disease and illnes This prevalent association has led to stereotype (e.g., senile crocks, old fossils; senescent, recalcitrant, intractable old fogies!). Many old peopl passively assume these roles.[17] In contrast t "aging-deterioration" models, this paper attempt to relate sensory, perceptual and performanc changes in later life to a functional, efficienc model of human aging.

Psychology of Aging

Gerontology is defined as the study of aging This field has as its primary focus over 20 millio persons in this country presently beyond age 65 This group has increased seven times since 1900 and by the year 2000, one in nine Americans wil be 65 or over. About five percent of this population are in institutions, and at least three-fourth live independently in communities. Curiously about 8% are institutionalized in Minnesota. Consonant with increasing longevity is the notion o prolonged human development and maturation More persons are experiencing continuation o their lives into what Erickson,[8] Havighurst[11] an others have popularized as "developmenta phases" of later life.



Figure

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*Excerpts read at the 120th Annual Meeting of the Minnesota State Medical Association, May 25, 1973, Bloomington, Mn.

†Former Assistant Professor, Departments of Family Practice and Psychiatry (Health Care Psychology), University of Minnesota Hospitals, Currently Special Services Consultant to the Ebenezer Society of Minneapolis.

Dedicated to the author's efficient and understanding doctoral advisor, Dr. Robert G. Warnken.

Almost a century ago, Sir Francis Galton used chronological age as a dependent variable in his anthropometric studies. He is credited with beginning a psychology of individual differences which has as its focus relationships among overt, measurable aspects of behavior and human characteristics such as age. For convenience, recent psychological research on human aging may be classified by three main sources of information about the aging: (1) What others report about the aging (e.g., family members, epidemologic surveys); (2) What the aging themselves report (e.g., the subjective or phenomenal aspects of aging); and (3) What researchers or trained investigators measure and quantify (e.g., task performance, empirical test data).

The psychology of aging has as its primary referent a conceptual matrix including the aging individual, the environment and their dynamic interaction, summarized in the Table. The aging person continuously changes and adapts in terms of biological capacities and experience, self-image and expectations, to an environment with physical characteristics (e.g., proximity of needed goods and services), family, significant others, and society in general.[14] Havighurst[11] regarded the social setting (environment) as providing a set of possibilities from which one can work out a pattern of aging that uniquely accommodates the person and is approved or tolerated by society. Examples of situations to which older adults frequently must adapt are diminished health or vigor, loss of spouse, retirement, altered social roles, and reduction of income.[9] Adjustment for an aging person may be positive or negative. Adjustive behavior has a biological base or substratum; that is, one's physical condition directly influences and determines amount and quality of behavior.[12,13]

TABLE
ADJUSTMENT FACTORS IN LATE LIFE

Aging Person	×	(Adaptation)	×	Environment
Capacities				Physical Parameters
Background				Family
Self-valuation				Significant others
Expectations				Society

Physiology, Perception and Performance

Though physiological aging processes are complex and differentiating normal from pathological age changes remains equivocal, biological aging or senescence is a universal, inevitable, irreversible phenomenon for each living organism.[19] Even more complicated is the proposition that aging is synonymous with differentiation. Individual differences *increase* with chronological age.[1-3] Outward signs of arcane aging processes such as graying hair, stooped posture, and skin changes are associated with invisible, internal alterations demanding specialized assessment (e.g., laboratory or psychometric tests).

Basic to psychological adjustment and behavioral efficiency at any age are those sensory and perceptual processes with which one negotiates his environment.

Sensation: Awareness of simple stimuli such as light or noise.
Perception: Meaning given to a set of (complex) stimuli.
Threshold: Amount of stimulus of the smallest magnitude that produces a sensation.

Receptors in the peripheral sensory apparatus enable one to organize stimuli above certain thresholds into sensory experience which may be consciously perceived by the individual. Although these processes are difficult to research and interpret across age groups, investigators seem to concur that reduction in sensation occurs with advancing age, marked beyond age 70. Further, stimuli thresholds generally increase in later life. Age changes, however, are enormously variable.[20] For example, the lens begins to lose elasticity and accommodation at about age 25 while auditory acuity diminishes as early as age one.[22]

Important adjustive functions of vision and hearing show characteristic age changes relevant to personal functioning in late life. As lens accommodation and pupil diameter decrease, quality and quantity of light diminish, resulting in less visual acuity and light-dark adaptation. Yellowing of the lens tends to filter out dark colors, with light tones better perceived. Aside from those with eye diseases (over one-half the blind are age 65 or above), the average older adult requires eye glasses, large print, high illumination thresholds and generally more time to light-dark adapt, important to such tasks as night driving.

Changes in frequency and intensity of sounds, such that auditory acuity diminishes, are not unusual in later life. Higher frequencies (over 10,000 cps) are lost or "filtered" first, especially in old men, suggesting genetic (sex-linked) or environmental (job noise) influences. Auditory thresholds increase so that effective verbal communication with the older person may require slower, articulated, modulated speech.

Other sensory mechanisms have received less attention. Smell and taste show age decrements with some evidence for tart, seasoned food preference as opposed to sweets. Proprioceptive, kinesthetic, thermic, pain and other sensory processes tend to diminish in acuity.[29,25]

Perception has been defined as *meaning* ascribed to complex stimuli. Inquiries regarding what the aging perceive relate to matters of daily adjustment and special functions such as work. Studies usually require the older subject to make measurable "sensory-perceptual-neuromotor" or psychomotor responses to complicated situations. Although the nature of the stimuli or task determines appropriateness of response (e.g., timed vs. untimed), aging adults—compared with younger persons—generally perceive and respond more slowly, less accurately (particularly to novel and/or ambiguous stimuli), more rigidly and appear to under-estimate the passage of time.[24] While these findings may not be surprising, it is important to keep in mind a wide range of individual differences in the aging population.

In studies of learning, older adults fare less well than younger persons. Due perhaps to diminished sensory acuity and primary changes in the central nervous system, the aging generally discriminate stimuli less and conversely, generalize more, resulting in "simplified" behavior. Generally, older adults take more time to acquire (learn) and extinguish (unlearn) responses; nevertheless, they certainly *do* learn. Learning is enhanced by simplification, repetition, frequent rewards and feedback, diminished competition and self-pacing.[6]

Performance on conventional tests of intelligence appears to decline with advancing age. Speed, task complexity, scholastic items, examiner bias and unfamiliarity with tests are some of the contributing factors. Cultural-experiential-verbal skills seem to be maintained well into later life, while perceptual-psychomotor performance diminishes.[5] With some qualifications, such tests as the *Wechsler Adult Intelligence Scale* are valuable in evaluating the older person's abilities.[16]

Age changes in sensory, perceptual and performance levels importantly modify overall behavior such that the older person may be characterized as follows: He behaves more *slowly, less* and more *uniquely* or selectively (including inaccurately or inappropriately). He may also be *less aggressive* and *less directed* in relation to external demands and constraints appearing to be highly invested in routine, daily tasks. These general behavior patterns may be construed elsewhere as dynamic, "personality" variables.

Efficiency Model of Aging

Overt, measurable behavior of older adults can be related to such criteria as adjustment and efficiency. As noted, psychomotor performance involves a complex chain beginning with sensation and ending with an adjustive response. To explore *causal* relationships among descriptive findings reported herein, a useful paradigm, the "efficiency model" (EM) is proposed.[3,24]

Analogous to computer systems, human behavior can be described as having input, processing, output and feedback components; in human terms, sensing, perceiving, behaving, and learning, respectively. Singly or in concert, these components influence behavioral *efficiency* and ultimately effect personal adjustment. The EM paradigm is expressed in the Figure. Peripheral sense organs are extensions of and integrate with the central nervous system. Sensation (A), above a threshold is centrally perceived or processed (B), resulting in an effector or output response (C), with subsequent feedback or "learning" (D).[4,6,21,24]

Practical Implications

Age changes in perception and performance may be regarded as developmental consequents revealing a wide range of individual differences. Intervention can occur in the Figure at all points (A-D). Diminished acuity and vigor can be compensated internally (e.g., learning, denial, attitudinal change, acceptance). Losses must be interpreted in view of importance to the aging individual. External compensation vis a vis prosthesis, eye glasses, hearing aid and other apparatus is not uncommon in maintaining adaptive abilities of the older person.

In view of increased individual differences in later life and lack of complete knowledge of perceptual-motor processes despite the EM, additional guides for geriatric practice include: (1) Advising thorough, highly individualized evaluation and treatment; (2) Behavioral or functional assessment, especially relevant to daily maintenance tasks; and (3) Prescribing prostheses including alterations of the older adult's personal environment where warranted.

Summary

Overt, measurable changes in sensation, perception and psychomotor performance show a range of individual differences and general decline with increasing chronological age. An "efficiency model" is presented to conceptualize and interpret relevant research and suggests provocative issues in the psychology of aging. The physician may enhance adjustment of the older adult by including knowledge of perceptual and psychological changes in geriatric consultation.

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President's Letter—Minnesota Was There (Page 605.)

The Minnesota delegation headed by Dr. Jack Pewters with Drs. Beck, Carryer, Kelly and Martin as regular delegates and Drs. Adson, Flom, Lester, Regan and Steiner as alternates, served with distinction during the five rigorous days. They were dedicated and effective and displayed great zeal and intelligence in representing the people and physicians of Minnesota.

On the last day, elections to the Board of Trustees produced after prolonged balloting—thirteen separate ballots—a dramatic change in the make up of the Board. There were eleven candidates running for the six vacancies on the Board of Trustees. Campaigning for these positions at times reached a furious pace. This is most amazing when one considers that a trustee spends approximately one hundred-fifty to two hundred days on AMA business away from his practice. The familiar charge that the AMA Board of Trustees is a self-perpetuating group of old men could not be farther from the truth, since the delegates elected five new trustees. This can not help but produce significant changes in the attitude of the Board. Such marked change in the Board of Trustees of the AMA is only possible in a healthy democratic organization.

Bernard Hall M.D.
President
Minnesota Medical Association

Common Psychiatric Syndromes of the Aged

FLOYD K. GARETZ, M.D.*

THE INCREASE IN the number of older people in our society and the greater incidence of emotional and mental disturbance in older people is resulting in all medical practitioners seeing many older patients with psychologic problems. It is my purpose to help the practitioner in recognizing these conditions and making appropriate dispositions or instituting appropriate treatment.

I will outline the most common psychiatric problems seen in older patients attempting first to outline the syndromes, and their treatment and secondly to indicate the main points in differentiating the syndromes.

The most common psychiatric conditions seen in older patients are as follows:

1. Acute Brain Syndrome
2. Chronic Brain Syndrome
3. Depressive Reactions
4. Psychogenic Thought Disorder
5. Alcohol and Drug Abuse

Brain syndromes are organic conditions characterized by impairment of intellectual function. They occur in all degrees of severity from subclinical to almost total loss of function and can occur with or without psychosis.

Although I will use the terms Acute Brain Syndrome and Chronic Brain Syndrome in this presentation, I must say that these terms, although commonly used, are in my opinion, misleading and unfortunate. First, they tend to be wastebasket terms that encourage too flippant labeling and disposition without adequate search for and clarification of etiology. Secondly, acute and chronic are misnomers because acute really is intended to mean reversible and chronic to mean irreversible. Inspite of my quarrel with these terms, I will use them.

Acute Brain Syndrome

The most important concept in acute brain syndrome is the concept of delirium. Delirium is defined as a psychologic disturbance characterized by:

1. fluctuating level of consciousness
2. visual hallucinations and illusions
3. fleeting delusions
4. impairment of all mental processes including orientation and memory
5. incoherence
6. changes in motor activity

The term "confused" often used to describe the delirious patient is nonspecific and probably best not used in this connection.

The patient with Acute Brain Syndrome appears and usually is physically ill. He will most often be seen on medical, surgical or neurologic wards rather than on a psychiatric service. Since the etiology of acute brain syndrome is physical, there are most often attendant physical signs. In older patients, the most frequent causes of acute brain syndrome are drug intoxication, decompensation in one of the major organ systems (such as cardiovascular, heptic, or genital-urinary), anemias, and malnutrition. In a large proportion of the cases, the etiology is multiple. The careful physical evaluation of all physical systems to uncover the multiple etiologic factors is of prime importance in the recognition and treatment of the acute brain syndrome in the older patient. Treatment, therefore, is of the underlying cause. For example, the discontinuation of medication such as barbituates and tranquilizers, instituting a proper diet and treating the anemia often is highly effective in reversing an acute brain syndrome.

Chronic Brain Syndrome

Chronic Brain Syndrome is a major source of psychiatric morbidity in older patients. The most important concept to understand in Chronic Brain Syndrome is dementia (i.e. intellectual deterioration). The following are the main characteristics of dementia:

1. Impairment of orientation especially for time

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See editorial, page 650.

and sometimes for place and person

2. Impairment in recent memory and recall with remote memory generally intact
3. Impairment of concentration, comprehension, attention, and judgment
4. Auditory hallucinations
5. Emotional lability

The most frequent types of Chronic Brain Syndrome seen in older patients are senile dementia and Chronic Brain Syndrome secondary to cerebral arteriosclerosis.

Many somatic and pharmacologic treatment approaches have been suggested for chronic brain syndrome in the aged such as cerebral vascular dilators, enhancers of cerebral metabolism, hyperbaric oxygen treatment, anti-coagulant agents, procaine injections as well as a variety of so called rejuventors. To the best of my knowledge, these are not very effective approaches, although certain stimulants and anti-coagulant treatments appear to be of some value in less severe cases. The best treatment approach appears to be environmental and social with emphasis on the protecting of the patient from such things as physical injury, being victimized, improper diet, self neglect of medical treatment and so on; also settings which may maximize social and personal interaction tend to lead to the highest level of mental and physical behavior for the patient.

Depression

When one considers the entire spectrum of severity, depression may be the common psychologic disturbance in the aged. Depression can best be understood as a syndrome of somatic, psychic and behavior signs and symptoms.

Common somatic signs and symptoms of depression are:

Anorexia
Insomnia
Fatigue
Reduced libido
Constipation
and Headache

Common psychic symptoms are:

Sadness
Irritability
Feelings of Guilt
Pessimism
Loss of Interest
Difficulty in Concentration
Suicide thoughts
Somatic concerns or delusions

Common behavioral manifestations are:

Crying
Motor retardation or agitation
Poor grooming
Withdrawal
Self reproach and Suicide Attempts

In the aged, depression differs somewhat from the typical depression of the younger adult. The onset is likely to be more gradual, it is likely to be primarily somatic in its manifestation, therefore being easily confused with the physical illnesses that are also so common in the older patient. Depressed older patients often show greater impairment of concentration and comprehension than younger adults, thus being confused with the chronic brain syndrome. The psycho-social etiology of depression is the occurrence in a depression-prone individual of multiple losses experienced or feared by the aged such as loss of health, loss of spouse, relatives and friends, loss of role in retirement, loss of financial security, loss of familiar physical surroundings and fear of the ultimate loss, loss of life.

I believe depression to be highly treatable, whether treatment be somatic such as electroshock treatment or anti-depressant medication or psycho-social therapies which emphasize re-establishment of self-esteem in the older patient.

Psychogenic Thought Disorder

The two most common types of psychogenic thought disorder seen in older patients are: (1) chronic long standing schizophrenia and (2) late occurring paranoid states. Chronic schizophrenia is characterized by recurrent episodes of psychosis (delusions, hallucinations, and bizarre behavior). The onset of schizophrenia is often in the late teens or young adult life so that by the time a patient has reached the 6th decade he may have a 40-50 year history of illness. Late occurring paranoid states of the elderly represent a first time occurrence in the 6th decade or later of a psychotic illness characterized by delusions and hallucinations of the grandiose or persecuting type. Psychogenic thought disorder responds favorably to antipsychotic medication such as phenothiazines and often can be treated with a short hospitalization.

Alcohol and Drug Abuse

Addiction and/or abuse of alcohol and other chemicals are more common in the older age groups than was formerly believed. A number of "hard core" alcoholics and drug addicts survive to old age and continue to be addicted. The long term alcoholics frequently reside in apartment complexes for the aged and create an ongoing problem in management for the housing authority and personnel working in the complex. These patients often resist treatment. Long term addicts are less visible to society having learned to stay out of trouble with the law and to avoid street drugs which are often contaminated.

Other patients who abuse alcohol and drugs are those who manifest the problem for the first time in old age. These patients most often use alcohol and drugs to deal with the anguish and depression they experience related to alienation and loneliness. This group of patients is highly treatable by both psychologic and pharmacologic interventions.

Differentiating the Common Psychiatric Syndromes in the Aged

An attempt will be made to delineate the main differentiating characteristics of the common psychiatric syndromes. The following four diagrams will summarize main points of differentiation:

DIAGRAM 1

Organic Versus Psychogenic Syndromes

	Impairment of Orientation & Memory	Impairment of Concentration & Comprehension	Presence of Delusions
Organic	+	+	+
Psychogenic	−	+	+

DIAGRAM 2

Acute Brain Syndrome Versus Chronic Brain Syndrome

Acute Brain Syndrome	Characterized by Delirium	More Likely Short Duration	More Show Improvement
Chronic Brain Syndrome	Characterized by Dementia	More Likely Long Duration	Less Show Improvement

DIAGRAM 3

Senile Dementia Versus Cerebral Arteriosclerosis

Senile Dementia	Progressively Deteriorating	Do Not Usually Show Emotional Lability	Seldom Show 2° Depression
Cerebral Arteriosclerosis	Episodic	Usually Show Emotional Lability	Often Show 2° Depression

DIAGRAM 4

Depression Versus Paranoid Conditions

Depressed	Self-Blaming (Intra-Punitive)	Somatic Concerns or Delusions	More Often Low Self-Esteem	Affect of Sadness
Paranoid	Accusatory (Extra-Punitive)	Suspiciousness and Delusions of Persecution	More Often Grandiose	Affect of Anger

My guts they yawl, crawl, and all my belly rumbleth;
*The puddings cannot lie still; each one over other tumbleth.**

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*Gammer Gurton's Needle. Act II scene i. 1575.

Access to the Interior Life of the Aged

JOHN P. BRANTNER, PH.D.*

THE PHYSICIAN AND NOVELIST, Gabriel Fielding,[1] spoke admiringly of "the splendid old." If we approach the medical and social and mental problems of old age in the context of physical medicine and rehabilitation, we can see more clearly those factors that make the difference, given equal disability and dysfunction, between those people who become progressively handicapped and those who make a splendid adjustment to the disability, pain, poverty, social isolation and disintegrated dying which our society makes the all too frequent lot of its elderly citizens.

We can, with great profit, study the factors that make the difference. We find that the most splendid old are very often crippled in body, poor in money, disadvantaged in power and status. They are often inefficient, in that they must expend more energy simply to accomplish everyday tasks like dressing, preparing meals and dealing with the bureaucratic demands of their world.

The source of their splendor is not in their exterior conditions, but in interior factors. The difference is not evident to census takers or property assessors. It is missed sometimes by physicians and others in health care. It lies in such invisible things as motivations and desires, expectations, attitudes, beliefs and characteristic definitions of self. The most significant thing is that these factors can be manipulated—we can change them for many of our elderly patients and clients.

There are four psychological factors that appear again and again in studies of old age, as well as in studies of psychological contributions to recovery from illness, slowing of terminal progress, adjustment in disability, and similar situations.

1. Those who adjust well to these conditions are generally free from undue depression. They learned early that the passions are in our control and that we can manage our own morale. They refuse to accept discouragement as an appropriate response. They know, like prisoners of war who survive *their* malnutrition and mistreatment, that we must do what we can to maintain our own morale. They shame us, sometimes, by their bravery, accusing our self-indulgent petulancy. In working with the aged we can focus on the sources of trust and hope. We can expose them in group situations to the contagion of hope.

2. The splendid old faced with distress and temporary discouragement have learned to share it with others. If they are friends, or if we love them, we take some of this burden in sympathy and understanding. If they are patients we too often see them as self-pitying, filled with unnecessary complaints. We may drive them to extremes of hypochondriasis, of grumbling and even to pain, before we are willing to listen. The wisest of them know this. Florida Scott-Maxwell recorded the following in her diary at age 82:

> "Our sorrow is such a burden for others. If it were possible it might be best to show nothing, and this is often tried with arid results, for it is unreal, inhuman. You express some of your unhappiness, partly to rid yourself of a little, and partly because honesty itself demands some expression. Expressing sorrow helps you to take it in, to know it better. But soon, soon you must claim it as your own, relieving others of its weight, so that they can say happily, 'Better today? All right now?' It is what they need to say, and you must answer brightly, 'All right, thank you'."[2]

3. They are active, restless and careless of their diminishing energy resources. They refuse to listen to us when we advise rest, quiet, calm and peace. They sense that inactivity speeds decline, that the renewal of health does not come with bedrest but with ambulation and exercise. When we say, "You must take it easy and rest," they know that they must not, and they walk to church in all weather, do their own shopping and indulge in orgies of house-cleaning or yard work. As Florida Scott-Maxwell said, "We urge now this, now that part of our flagging bodies, and when

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we have spurred them to further functioning we feel clever and carefree."[3]

They do this with increasing determination as disability grows more. (Do we murmur "stubbornness," "agitation," you and I?) "Age puzzles me. I thought it was a quiet time. My seventies were interesting, and fairly serene, but my eighties are passionate. I grow more intense as I age."[4]

4. The splendid old are rich in acquaintance, reaching out for sustaining and mutually rewarding relationships with companions and friends who must of necessity, if they are newly added, be younger by one, two, or even three generations. They refuse the isolation we offer them and do not accept loneliness. Retired school teachers may be bitter and cynical for they are usually poor and frequently disabled. *But* they are rarely lonely. They learned early the art of speaking the language of the young and of liking people in the generations that followed their own. They know in their eighties how to find 60-year-old and 40-year-old friends. This ability serves them well and it is one we can teach our elderly and lonely patients. It is one we can learn ourselves.

There are a number of ways we can come to an increased professional understanding of the aged. Perhaps the best way to obtain glimpses of the interior life of the elderly is through perceptive social involvement with them. Most of us have our major social contacts with our own generation. We depend on blood ties for relationships that reach across the generations. It is always useful to be deliberate about adding to our acquaintance and we can seek out friends one and two generations older as well as staying open to significant growing relationships with the young.

The humanities can contribute richly to the health sciences, and we can learn much from the perceptive study of what the poets, novelists, and playwrights have said about old age. How greatly King Lear deepens our awareness of the interior world of the paranoid, threatened and deteriorated old man. Emily Dickinson says as much in eight lines as many sociologists say in eight chapters:

"The harm of Years is on him—
The infamy of Time—
Depose him like a fashion
And give Dominion room.

Forget his Morning forces—
The Glory of Decay
Is a minute Pageant
Than least Vitality."[5]

This echoes more elegantly the remark of an old man who was heard to say: "I knew old age was going to be bad, but I didn't think it would be this bad."

Lastly, as we grow older ourselves we can practice a sensitive awareness of the interior aspects of our own aging, rather than denying it. This last is especially important. What I do for many disadvantaged groups is good, but not directly rewarding. What I do to increase the understanding of the problems of the aged and to ameliorate their condition rewards me directly and concerns me deeply. It is certain that I shall be either dead or a member of this currently disadvantaged and misunderstood group.

In our society, old age is mostly a time of poverty—poverty of money, poverty of time, poverty of strength, and poverty of relationships. What we do to alleviate the condition of the aged contributes directly to the improvement of our own future.

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Francis Tyce, M.D.

Dr. Francis Tyce, medical director of the Rochester State Hospital, has been named the single chief executive of the hospital, ending the running of the hospital for more than 10 years by more than one official.

Medical Management of an Aging Population

JESSE J. BARRON, M.D.

Every day about 4,000 Americans reach their 65th birthday. This figure, when offset by the death rate, means that the elderly population is increasing at the rate of 1,000 persons per day. At this time the older population represents over 20 million Americans 65 years of age or older which is about 10% of the total population of the United States. While this 10% figure appears small, it represents over 25% of the health care delivery in this country. Thus the physician's understanding of the problems and the health needs of this age group is extremely important if the expended amounts of time and cost are to culminate in an appropriate increase in comfort and dignity for the patient.

The philosophy of geriatric medicine is the problem of differentiating between an ill and an aging person in order to avoid serious problems of management. An older person is often considered to be ill rather than undergoing natural physiological changes. A person who is frail, forgetful, repetitive and boring, selfish and perhaps concerned about death is not ill. This is as normal as a comparable behavior of childhood. Medical personnel must reject a rather classical orientation in our culture to the "sick old man." The physician must think, speak and describe in accurate terms to avoid labeling patients as senile when in actuality they are reacting normally within the restrictions of their age. Disabilities abound in the elderly, but disabilities are not necessarily active disease. Surgical and medical procedures which were formerly considered radical for the elderly should be determined solely within the context of risk and benefit to the patient. The healthy patient could become an invalid and the independent citizen a public charge.

In a recent study of octogenarians who came to autopsy, the correct cause of death predicted by the attending physician was made in 50% of the cases, partially correct in 17% and totally incorrect in 33%. These figures indicate that a significant number of patients could have lived had appropriate studies and treatments been attempted without arbitrary decisions being made on the basis of age.

It isn't enough to prolong life just for the sake of prolonging life. The biological depreciation, loss of role, self esteem and social worth in the elderly become intolerable. There is no point in adding senile years. The biologist tells us that we now have the potential of adding about 20 years of vigorous adult life to our existing span by utilizing present knowledge of preventive medicine measures in the control of blood pressure, diabetes, arteriosclerosis, cancer and body temperature regulation. The genetic mechanisms in the aging process are so well understood now that it may be feasible to exceed 100 years of active life by the year 2000. While these facts seem incredible at the present time it requires a vigorous approach by the physician in assessing his role and knowledge in the preventive measures available today.

Medical management of the elderly must include an understanding of the dietary and metabolic needs in this age group. We have an almost instinctive appetite for the pleasures of eating, but the desire for food does not decrease with aging proportionately to the requirements of the body. In addition to the lower metabolic needs, an older person, by the very nature of his existence, becomes less active and accordingly requires less nourishment. By the age of 65 the caloric requirement as a whole should not exceed 1500 calories if an appropriate weight is to be maintained. We also have to consider the pos-

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sibility of the effects of hypoglycemia in patients on the brink of senility. It is reasonable to assume that a three meal a day program, while capable of supplying the necessary 24 hour nutritional requirements, allows for a significant drop in blood sugar values in widely spaced meals. It means that marginally performing patients may exhibit confusion and belligerency during the state of hunger. Physicians and businessmen also may be effected in their judgment if a protracted period of time exists between nourishment. For this reason a five meal a day program has been recommended by many nutritionists and geriatricians. It is a method by which an individual can maintain a more appropriate weight as well as a more constantly productive physical and mental state.

A century ago when physiotherapy programs were not available, conditions in the elderly were compounded by the loss of muscle tone with atrophy and the ever present danger of contractures. Along with this kind of inactivity there is the problem of secretion accumulation in precipitating pneumonia. Other by-products are constipation and a high blood concentration of calcium salts due to the osteoporotic process with resultant kidney and bladder stone production. There is increased incidence of pressure sore formation, phlebitis and the instability of the cardiovascular system, predisposing to the symptoms of orthostatic hypotension and instability of gait. All of this can best be summed up by a poem by R. A. J. Asher entitled "The Dangers of Going to Bed" from a British Medical Journal of 1947:

> Look at a patient lying long in bed
> What a pathetic picture he makes!
> The blood clotting in his veins,
> The lime draining from his bones,
> The scybala stacking up in his colon,
> The flesh rotting from his sweat,
> The urine leaking from his distended bladder,
> And the spirit evaporating from his soul.

Among the major pitfalls in medical management of the elderly is the prescribing of drugs. Since older people generally have a higher incidence of illness it is natural to expect a greater number of drugs to be prescribed for them. This fact makes it essential to understand the problems of aging in the context of the nature of the drugs prescribed. Some of the more common physiological changes accompanying aging that affect the action of drugs are loss of muscle mass and alterations of function of the cardiovascular, renal, respiratory and central nervous system.

The muscle atrophy of the elderly may not be obvious because of the prominence of the fat distribution, but it represents a significant effect in reducing drug dosage requirements. Toxicity by over-medication in this age group is extremely common. Decreased kidney function, beginning at about the age of 30 and continuing in a linear decline as measured by creatinine clearance, renal plasma flow and glomerular filtration rate, represents another important factor since most drugs, at least in part, are excreted by the kidneys. This is especially true when prescribing Digoxin and the Aminoglycosides such as Kanamycin and Streptomycin. With reduced numbers of functioning brain cells the usual therapeutic dose of sedatives and tranquilizers can become overwhelming with symptoms of central nervous system depression, ataxia, confusion and postural hypotension. In my own personal experience I have found that the effects of barbituates in older people often is more stimulating than it is sedating. The precise mechanism for this is not known although the aging process does alter individual neurones with a slowing process of the conduction impulse. The adverse affects of anticholinergics in the older populations is well known in precipitating the mydriatic change leading to glaucoma and causing urinary retention in both males and females. Reduced cardiac output associated with the changes of aging can significantly reduce the dispersion of the drugs and localized arteriosclerosis may prevent adequate distribution of the drug to a specific part of the body.

Very commonly seen are the older patients who have problems in communication. This becomes a real art comparable to the practice of veterinary medicine. Is the patient cerebrating adequately to comprehend oral instructions? Is his hearing capable of receiving the spoken word, is his vision adequate for reading medication labels or properly filling an insulin syringe? Last, but not least, does he have a reasonable grasp of the English language? If all of this isn't enough to challenge the patience of the conscientious physician, how do we know that the patient is following the prescribed instructions? He may take two tablets because one didn't seem effective, or perhaps he stopped the medication altogether because he was feeling better. Some patients use laxatives so excessively that it causes a flushing of the gastrointestinal tract that inhibits the absorption of medications. These may sound like simplistic and rather easily identifiable facts, but t has been my experience in practicing Geriatric Medicine, that they are also easily ignored in prescribing medications.

I would like to introduce at this point a subject which generally is met with resistance by physicians, para-medical personnel and the general public. It is the subject of sexuality in older people. These older people themselves share the fears, apprehensions and taboos which arise when the subject is introduced. The concept of the "dirty old man" in our culture is quite deeply ngrained, evidenced by jokes, colloquial expressions, suspicions and a general attitude that is not only demeaning but frequently condemnatory. Due largely to these factors, no sample of older persons has yet been studied which would be broad enough or representative enough to supply us with an adequate system of norms. However, responsible sexologists including Masters and Johnson, Kinsey and the Duke University Center for the Study of Aging and Human Development are exploring this area and raising questions as o the validity of the generally held feelings of hose working with older people. In their opinion, sexuality, in both its broad and its specific form, remains an important, and in many cases a lifelong consideration in this age group. I have found this borne out in my clinical practice. I feel that it is a real challenge to physicians to not only draw upon the available knowledge without prejudice, but to encourage their patients toward an open and non-demeaning discussion of their sexual needs and practices.

The utilization of various community resources can be extremely helpful in maintaining continuity of care of the patient. Visiting nurses can determine whether the patient is taking medication as prescribed and noting benefits or adverse reactions in the treatment program. More recently, the physician associate has been trained in a program to assist the physician in a manner that complements the nurse's performance by enabling him to do complete histories, physicals and to prescribe treatment within the limitations of his training. It has good potential for the physician's ability to extend his care beyond the hospital and office practice. This area is still in its infancy but is showing promise in my opinion, for improving the health delivery program.

Our preoccupation with self-sufficiency often makes us, as physicians, resentful of the disabled and elderly patient. We feel the incurable and the old as threatening and castrating objects. As a result, the older patient feels the rejection by the physician, and his frustration, anger and depression become even greater. Our concern and management of the elderly reflect the validity and constancy of our concern for the essential dignity of human life.

Southern Minnesota Medical Association's Annual Meeting

This year the Association will meet September 21 in Judd Hall in Rochester. The program will be printed in the September issue.

Amnion Graft

The Young Helping The Aged

JOSEPH E. ADDUCCI, M.D.*

Amnion grafts have been used in degrees for peripheral vascular disease, burns and now to aid in the healing of denuded areas when a patient is too disabled and too poor a surgical risk for a split thickness skin graft.

For thousands of years the young have given aid to the elderly. A relatively new example of this help is the use of amniotic membrane as a hemograft to assist in the healing of the wounds of the aged. This procedure can be performed without the anesthetic which can be so life threatening to the aged. Although this type of graft is not meant to replace the skin graft in every instance, it can be used as a temporary covering to decrease fluid loss and prevent infection, or to aid in the closure of a wound defect when the patient is a poor candidate for anesthesia and skin grafting.

The healing properties of implanted amnion have been reported in the treatment of peripheral vascular disease with varying results.[1,5] It has been suggested that some illusive factor exists in human amnion that can alter the course of this disease in an unpredictable fashion. Amnion grafts have also been used for primary burn dressings with good success, and as an aid in the covering of a burn too large to be adequately handled by skin grafts.

The amnion consists of a low cuboidal and mesenchymal cells and has very little antigenicity and hence very little host rejection. The amnion should be separated from the chorionic membrane which has a relatively high antigenicity. This is easily accomplished at the time of delivery by blunt dissection.

It has been reported that amnion of the recently delivered infant can be preserved by freezing techniques, although with the readily availability of a maternity ward in most hospital this would hardly seem necessary. Preservatio beyond twelve hours can be enhanced by th addition of broad spectrum antibiotics to th saline preservation solution. After delivery, th membrane is washed with normal saline solution and stored in a refrigerator where it ca be preserved for twelve to eighteen hours.

In the delivery or operating room and unde sterile conditions the amnion is washed repeatedly with normal saline solution to free it of bloo cells that may remain. The amnion should b obtained from a noninfected gestation and preferably one in which the membranes were not ruptured many hours prior to delivery. The amnio from a vaginal delivery may be used provide sterile conditions were present, both from th standpoint of delivery of the placenta and th absence of antepartum material infection. cesarean section would be an ideal delivery fro which to obtain a sterile amnion.

The wound to be grafted is cleansed wit Betadine and irrigated with sterile normal saline The amnion is spread over the defect. The graf is held in place by several 000 chromic suture placed at the margins. Once placed only routin care of the graft is necessary using moist salin dressings. These dressings can be discontinue after the first week. The amnion sloughs at th border as the healing progresses. Portions of th graft are apparently still viable from fourteen t twenty-one days after the original grafting.

Case Report

The patient is a seventy-seven year old white femal whose original problem was a scirrhous carcinoma of the breast complicated by uncontrolled diabetes mellitus and severe hypertension. After confirmatory biopsy a radical mastectomy with axillary lymphadenectomy was performed. No positive nodes were obtained. Although the skin closure was without tension, four days after surgery an area of necrosis appeared at the center of the wound. Multiple debridements were performed and after two weeks, and area 16 cm x 10 cm with necrotic margins was bare to the chest wall. Over the next six weeks, cleansing and debridement were performed until the area appeared ready to accept a graft. At this time the diabetes was poorly controlled and the blood pressure was 240/160. Because of these problems the patient was a poor candidate for an anesthetic. The patient was, however, quite anxious that something be done about this raw area in the center of her chest.

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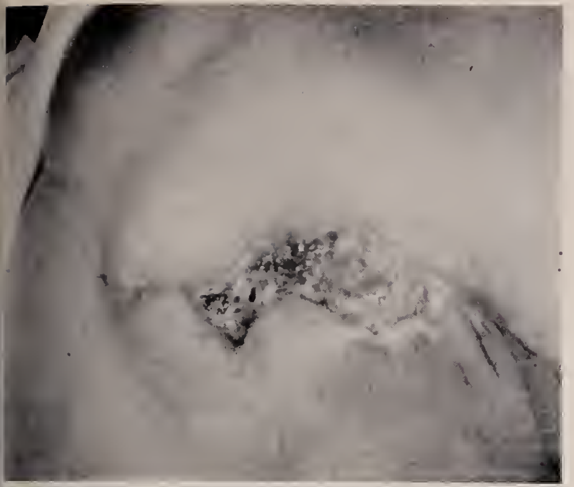

Fig. 1—Wound before grafting.

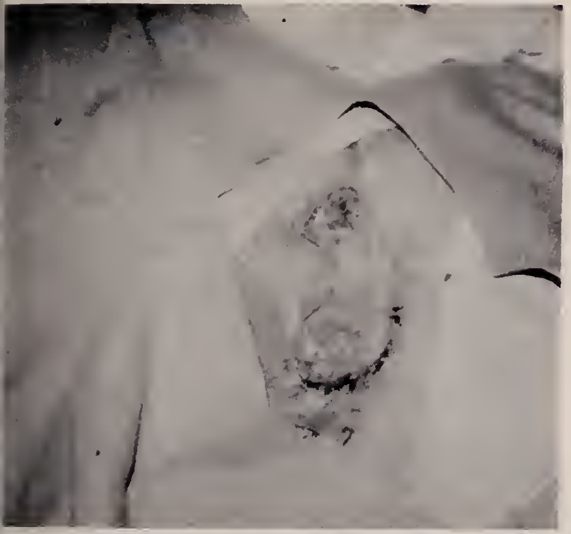

Fig. 2—Wound with amnion in place.

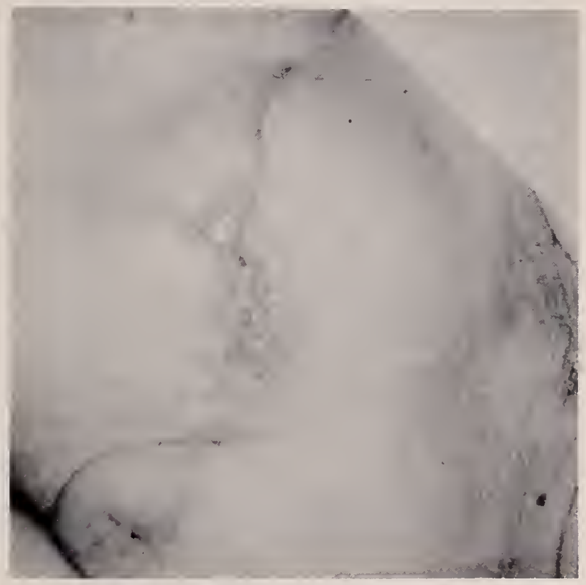

Fig. 4—Wound at two weeks.

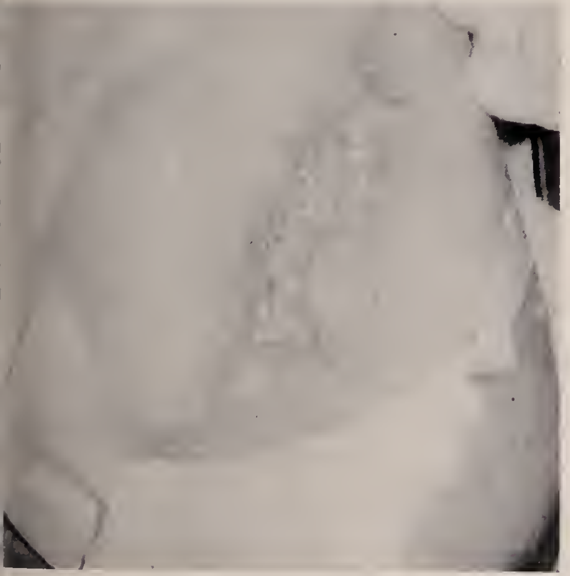

Fig. 3—Wound at one week.

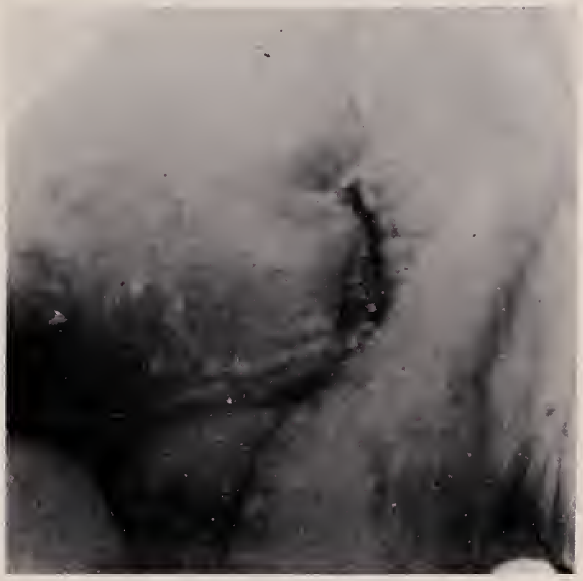

Fig. 5—Wound at three weeks.

An amnion graft was obtained from a newborn and after careful cleansing and washing was applied to the defective area. Unfortunately the patient was somewhat senile and removed the dressing to examine the wound. In the process, approximately half the graft was dislodged. The graft was reapplied the next day, and routine post-operative graft management was employed using warm saline dressings.

Photos, Figures 1, 2, 3 and 4, show the wound healing at the time of the original grafting and at one, two and three weeks after grafting. At three weeks the area is almost completely closed, with only an area of 1 cm x 3 cm still granulating. This area was completely closed at four weeks.

Discussion

The use of the amnion graft has been considered and used in varying degrees for peripheral vascular disease, burns, and now to aid in the healing of denuded areas when a patient is too disabled and too poor a surgical risk for a split thickness skin graft. It is suggested by this experience that the use of the amnion graft, although not intended to replace the skin graft could be used in such instances.

A case is presented in which the healing of the surgical wound of an elderly hypertensive, diabetic woman with a carcinoma of the breast has been aided by use of an amnion graft. Further experience with this kind of graft may uncover additional uses. This technique could be employed after wound breakdown following radical vulvectomy. It would not be applicable to a pressure wound such as decubitus ulcer, because the thin layer of amnion would most likely be disrupted. It is hoped that further work will be continued in this area and that in the future, the aged may continue to be helped by the newborn.

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Troell-Junet Syndrome

A combination of clinical entities that includes toxic and usually nodular goiter, diabetes mellitus, acromegaly, and hyperostosis of the cranial vault characterizes this syndrome. Troell of Sweden first reported two cases in 1938; Junet of Switzerland reported three cases in the same year and later added another; Moore described six cases observed in the United States.

All 12 patients were females whose ages varied from 23 to 73 years.

The changes in bone tissue are unusual and consist of intense osteogenic activity in both the periosteum and endosteum. The hyperostosis is diffuse and symmetric, most marked in the occipital bones, but may occur in the frontal area. The temporal bones are usually unaffected. In one patient described by Junet, there was a spongy character to much of the skeleton.

Etiology has not been established, but evidence strongly points to the pituitary. Hypophyseal adenoma was found at operation or autopsy in six of the 12 patients. It has, therefore, been presumed that the type and character of these bony changes are on the one hand a result of the anabolic effect of the hypophyseal growth hormone and on the other hand a response to the catabolic effect of the hypersecretion of the proliferating goiter.

Durham, Robert H.—Encyclopedia of Medical Syndrome
Hoeber Medical Division, Harper and Row, New York

Human Gerontology and Geriatrics

S. W. GEDGE, M.D.*

A glimpse of the wide panorama of geriatric medical challenges which present hemselves to us every day. This is a fertile field for the study of improved medical are delivery and research into the natural history of disease and the basic biological nechanisms of aging.

AGING IS A CONTINUOUS, probably normal rocess characterized by certain anatomic, physilogic, and biochemical alterations at the molecuar and cellular levels which, with the passage of ime, affect the function of all of the cells, tissues, nd organs of the body. These changes occur hroughout life but become more apparent during ater maturity (40 to 60 years of age), senescence 60 to 75 years), and old age (after 75 years). he changes of aging may be difficult to disinguish from damage due to disease, and, as a esult, disease is often mistakenly equated with ge. Some people may age so gradually that they nay not realize they are aging until they become l.

Man has a predetermined life-span, and his hances of dying increase significantly after the ge of 45. Human aging is accompanied by a ogarithmic increase in the death rate from disase, especially cardiovascular disorders, and dereased efficiency in homeostatic mechanisms.

Senescence, the normal process of growing old, a part of the life cycle experienced by people vho attain healthy old age. It differs from senility, vhich is pathologic old age.

Progressive biological changes during senesence alter the morphology of tissue, impair the unction of the cardiovascular system, interfere vith the action of the sensory organs, and produce gradual reduction in the physiologic functions f the body.

The introduction of actual disease into the ody accelerates aging and shortens longevity. In hysiologic death from old age, many elderly eople may die from insufficiency of a vital organ s a result of age related cellular depletion rather han from conventional physical and mental diseases.

The degenerative processes of aging occur whether the organism is subject to disease or not, and are primarily the result of cell losses throughout the body. Progressive loss of body cells is thought to be due to a decline in the body's capacity for self-repair and reproduction. Most men between the ages of 65 and 90 average a 20-pound weight loss. Between 30 and 75, hormone production declines, the kidneys show a 55 per cent reduction in efficiency and the speed of nerve impulses along single fibers declines 10 to 15 per cent. Muscle strength, maximum breathing capacity, and oxygen uptake all diminish by about 50 percent. The average weight of the brain falls from 1,375 grams at the age of 30 to 1,232 grams at 90. At the age of 75, the average heart pumps only 65 percent as much blood as at age 30; the brain receives 80 percent as much blood; the kidneys receive only 42 percent as much. The bones tend to lose their calcium salts and become brittle. The connective tissues of the body contract and harden, resulting in the characteristic stoop of old age. Lost cells usually are replaced by connective tissue, which partly accounts for the decreased amount of water in the body as it ages. The skin loses its elasticity and ability to retain water. Layers of fat directly underneath the skin gradually change and are no longer uniform, causing skin shrinking and wrinkles. The arteries harden, thicken, and lose their elasticity.

As a result of all these losses in reserve capacity, the organism finds it more and more difficult to adjust to changes in its environment. It takes longer to return to normal function after disturbances caused by disease, shock or accident, and the individual finally dies.

Thus, senescence is a deteriorative process which includes the sum total of those processes which lead with age to a failure of a person's ability to withstand stresses, injuries or changes. Our present state of knowledge of human gerontology is very limited and has great promise for future medical research.

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The modern physician is challenged and tested every day in his care of an increasing number of elderly patients. This composes the fascinating multidisciplinary field of clinical geriatrics. More than ever, the older patient requires the services and attention of a general physician who is concerned with the diverse problems of patients with multiple diseases in different stages and with multisystem involvement. A knowledge of the effects of aging on mental and physical functions, the natural history of disease, and the diagnostic and therapeutic tools available in modern medicine must be carefully coordinated by physicians deeply concerned for the suffering of elderly persons. In my experience with young physicians, I am impressed by the compassion most of them show for their elderly patients. However, there is a tendency for all of us to either under-react to the needs of aged patients and too quickly blame senility, arteriosclerosis and old age for potentially correctable medical states, or become over-enthusiastic with sophisticated, costly testing and prolonged hospitalization and therapy. Although the basic principles of sound medical practice pertain to patients of all ages, in the care of the aged the delicate art of medicine requires mature judgment and a deep compassion for the patient and his family, and for all the personnel involved in the care of the patient in his home, nursing home or hospital setting. The use of common sense in the evaluation of these patients cannot be over-emphasized.

It is my opinion that the physician is obligated primarily to relieve pain and suffering and not feel guilt or excessive anxiety when caring for terminally ill aged patients when all reasonable efforts to prolong life have been exhausted.

Most of the difficulties I have experienced and observed in the care of the elderly have been the result of preconceived notions regarding senility and old age, lack of thoroughness in history taking and physical examinations and over-interpretation of laboratory tests, all of which may lead to misdiagnosis.

A conscientious effort must be made to understand each patient as an individual, consider his past medical problems and social and occupational background, and carefully consider his present total social and economic setting and listen to his complaints and desires. Social maladjustments may sometimes present themselves as bizarre symptoms. His understanding of diet and prescribed medications may be confused. Alcohol or tobacco abuse may easily be overlooked. The significance of the complaints of the older patient should not be underestimated. Contrary to usual belief, older people do not complain enough so with old age there is a tendency to accept pain and discomfort as inevitable. Because many patients are reluctant to have others think of them as growing old, they first keep their complaints to themselves, accepting them as inevitable, and secondly resist efforts by their physician to obtain an accurate medical history. A thorough examination is obligatory since seemingly minor lesions are often found that may be potentially serious or may cause more discomfort or emotional stress than more serious disorders. The value of simple psychotherapy cannot be overestimated, as well as simplified, logical and honest explanations to the patient and family to allay fear and anxiety. In the long-term care of elderly patients, repetition of the medical history and physical examination helps to either reinforce or change previous diagnoses and makes future care more meaningful.

The clinical description of a number of elderly patients will help illustrate some important diagnostic points unique in the care of the aged.

An elderly farmer was hospitalized for a few days while his family physician made arrangements to commit him to a state hospital because of advanced senility. A careful history, examination and a few appropriate tests indicated hypopituitarism. Another so-called "senile" patient had advanced myxedema. Dehydration and electrolyte imbalance resulting from gastroenteritis, surgical procedures or aggressive therapy for congestive heart failure commonly result in mental alterations suggesting senility or senile psychosis. Reactions from drugs such as sedatives, hypnotics, and tranquilizers or antidepressants may suggest similar diagnoses.

One patient who was comatose for three days postoperatively following a nephrectomy with a diagnosis of possible cerebral anoxia from cerebral hemorrhage or infarction was finally discovered to have water intoxication from excessive

I.V. fluids. This patient had an uneventful recovery when this fact was uncovered.

An elderly man was hospitalized for four months for multiple strokes and at autopsy was found to have a brain tumor. Serial EEG's or an Echo recording would have been most helpful.

Another man in his late 60's had severe arthritis in both hips and one hip caused pain in his thigh when he walked one-half block but was relieved promptly by rest. He was found to have aorto-iliac arterial occlusive disease which was surgically corrected.

An insurance man who was semi-retired had vague personality changes noted only by his wife, and intermittent incoordination of an arm and mild ataxia. Neurologic exams including EEG's were inconclusive, and senile arteriosclerosis was diagnosed. When he became worse, bilateral subdural hematomas were evacuated, and he became completely normal. He could then tell us about a head injury which was not known previously.

It is not uncommon for patients with strokes to be found to have silent myocardial infarcts. Therefore, electrocardiograms may be valuable additions to stroke evaluations.

Occult malignancies of the genitourinary or gastrointestinal tract have been found in a number of older patients who were on anticoagulant therapy for cardiovascular or cerebrovascular disease.

Cardiac arrhythmias secondary to primary cardiac disease or from cardiac medication may result in syncopal episodes, seizures or neurologic changes in older patients. ECG monitoring, pulse and blood pressure records in supine and standing positions, and electrolyte determinations may be most helpful. Determinations of total and free thyroxine may help exclude thyrotoxicosis or myxedema. Blood digitalis levels may guide the use of digitalis when underdigitalization or toxicity are unclear. Electronic pacemakers have been most valuable in the care of selected patients.

Transient ischemic attacks and cranial arteritis are not uncommon problems in elderly patients with intermittent and often vague neurologic disorders, and should be considered because they are so readily amenable to therapy.

A careful pre-anesthetic medical exam is an important part of the medical care in older persons before any surgical procedure, to determine risk and find significant conditions which need careful monitoring during and after surgery. Severe hemorrhage, hypotension or arrhythmias during surgery require a thorough post-operative medical re-evaluation. Chronological age per se, as we all know, is not a contraindication to necessary surgical procedures.

Prostatism, urinary tract infections and other genitourinary problems in the elderly often require urethral catheterization or urologic procedures. In these individuals attention to the possibility of bacteremia and the early signs of bacteremic shock is important.

The newer fiberoptic techniques for examination, biopsy and treatment of lesions of the esophagus, stomach and colon may reduce the risk of major surgical procedures to diagnose malignant lesions and remove polyps high in the colon.

New Editor-in-Chief of MINNESOTA MEDICINE

Dr. Reuben Berman will retire as Editor-in-Chief of MINNESOTA MEDICINE at the end of this year, and the Council is interested in hearing from any physicians who would like to be considered for this position. It is hoped that a new editor can be chosen by September 15. Address communications to: Council, 375 Jackson St., St. Paul 55101.

R. J. Frey, M.D.
Chairman, Council

Retirement

Promise or Threat?

H. ETTA SALOSHIN, PH.D., A.C.S.W.*

COMPULSORY RETIREMENT is a common phenomenon in most modern day societies. It is usually set for a certain age—somewhere in the mid-sixties—regardless of the individual's physical or mental health, ability, performance, or preference. Few occupations or positions make allowances for alternative arrangements such as part-time employment, or reduction of work-load and hours. Retirement income, in the form of pensions, rents, or—as in our case—social insurances, are provided by states, by organizations of employing companies, by pension funds, or by combinations of these. Our system of retirement then is not dissimilar from those in other industrial nations.[1]

There are several significant differences. Cultural values affect the anticipation as well as the adaptation to retirement. In a society like ours where youth is considered the most desirable stage in development, all reminders of growing older are unwelcome. Persons who have to become dependent—financially or in other respects—after a life of independence, hold a low opinion of themselves in a culture that praises independence and productivity above all else.

There are also, of course, individual differences. Socio-economic, educational, and occupational factors play a significant part. Whether retirement is voluntary or compulsory is also an influential factor. The status of one's health and its psychological and financial consequences play an important role. Retirement preparation and counseling do affect post-retirement adjustment. The same applies to previously developed leisure time tastes and habits. Family relationships, especially within the marital pair and with grown children, all have a decisive influence. Of paramount importance is the meaning that work holds for the individual.

The Economic Side

At best, the retirement income of the economically most favored occupational section in ou country averages about 50% of the earnings o the immediately preceding years. For the majority of our older population, it is much lower, amounting to 20% to 40%. Although the average income of the entire group of retired persons in the United States is higher in terms of buying power than in any other country, the difference between a person's earnings and his retirement income is higher here than anywhere else. More than in any other country, the retiree here has to face significant changes in his living standard.

While it is true that certain expenses can be reduced, others rise. Indeed, one does not need as many clothes if one does not work and one can eat more meals at home, give up membership in associations, clubs, etc. While this saves money, it entails further curtailment of outside activities on top of other ongoing restrictions resulting from termination of work. One may have to pay for services that previously were free, for instance, insurance previously paid by employers. And, in spite of Medicare, expenses for one's health care are generally higher than they were before.

In any expanding economy, prices as well as wages and other earnings are on the rise, while the income of persons who are not part of the labor force does not keep pace. During an inflationary period such as we have now, this leads to a catastrophic lag for those with fixed incomes. To accentuate this further, most retirees are unable to find opportunities to augment their income. Furthermore, in our country, work involves forfeiting part of the only sure source of income, social security benefits. Retired persons today, find themselves financially in a multiple squeeze.

An additional harmful consequence of lowered income is its effect on self-assessment. We do measure our personal worth, at least in part, by the way in which we can compare ourselves with others. And the multiple squeeze exerts a continuous downpush on our sense of self-worth. Simultaneously, there are other aspects to cope with which, in turn, may have a diminishing effect on one's self image. If mastered successfully though, they may hold the promise for a rewarding completion of one's life.

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Coping with Many Tasks

Retirement, like other decisive changes in life patterns, presents the individual with challenges. It may constitute a crisis with threatening prospects. However, it may also be the beginning of a period with fewer pressures, lessened responsibilities, and greater freedom. In any case, it demands simultaneous adaptations in a number of vital areas and coping with a number of important problems:

1. The retired person and those immediately involved with him must arrive at decisions which have important consequences for the rest of their lives. These decisions concern financial matters, health care, and housing. Almost invariably, the move to another residence or community entails giving up possessions and parting with people.

2. We have to relinquish significant social roles. Foremost among them is our work role, the source of our main identification, prestige, and status.

3. Together with loss of the work role there occur a number of other separations:

(a) We become disassociated from our colleagues or co-workers. This seldom happens overnight. In fact, quite often, both parties wish to maintain their relationship and to stay in touch, especially during the first few weeks after retirement. The retiree frequents the places where he previously met his work friends, and usually is made to feel welcome. Eventually though, he feels excluded. People talk about that which they presently have in common, and as time goes on, the former colleague no longer shares in these common experiences. During our work life we interact more frequently with colleagues and in work related contacts, than with others. It is easy to recognize therefore that this disassociation leaves a major gap in one's social relationship.

(b) Equally important, especially for scientists, scholars, and professionals, is the fact that through interchange with our colleagues we gather knowledge, keep up to date with new developments, test our ideas, gain stimulation and encouragement for new professional exploration and endeavors. To be sure, one keeps up with one's reading, at least during the early phases of retirement. But what one has read takes on additional meaning as we discuss it with our peers, as we raise questions, or as we receive confirmation of our assessment and interpretation of that which was read. Thus, concomitant with the shrinkage of our social world, the separation from professional co-equals also may lead to a sense of being left behind, of being out of touch with that which goes on in one's field.

(c) Another effect of separation from work is spatial aimlessness. Suddenly, one does not have a place to go. Much as we may resent the daily trip to work in all kinds of weather, during the height of traffic, and perhaps at ungodly hours, when we have no destination at regular times, many of us show surprising reactions. For instance, without intending to, we may find ourselves on the familiar route to work. At other times, we invent good reasons why we should go to the old place, while, in fact, we just want to find out whether we still feel that we belong there. Or, we may carefully stay away, to strengthen the realization of the break with the past.

Being able to stay at home, to sit in the sun, to listen or to read, all those things that we had dreamed of in the past, and that we may have cherished during vacation time, just do not offer the pleasure which they promised while they were unattainable.

(d) Actually, the absence of a place to go, is part of the perplexing and unsettling phenomenon of use of time. Most of us are used to fairly regular schedules, and although they initially had been determined by outside forces, we eventually transformed these schedules into part of our own rhythm so that they function like "built-in-time clocks." We automatically wake up at the same hour every morning; our organisms crave food whenever our work routine had set meal periods; and we yearn for rest and relaxation or sleep after the store closes, or the factory whistle blows, or the last patient has been seen. Now, however, these schedules have become superfluous, our internal rhythm does not correspond to current external demands. Time does not need to be regulated rigidly, one can do with it as one wishes. Unfortunately though, few of us know what to do with it. When we are faced with a block of uncommitted time, we sometimes feel guilty, or else we have the nagging feeling that there is something urgent that we have forgotten to do. Most of us simply get restless.

Individuals with strong drives and inner compulsions—characteristic of a high proportion of executives and professionals, with physicians being in the forefront—are apt to reschedule themselves after the model of their most recent work life. They become active in organizations, associations, or clubs; they enter various movements and activities; and they seem to be constantly on the go. They may start and discard different ventures as they seek a substitute for the work which made them feel productive, successful, and wanted, and which demanded regulation of time. Sometimes this turns out to be mere "busyness," serving primarily as a time filler. Others though may be lucky enough to find activities that are meaningful to them or which engage them in efforts that contribute to the welfare of others. This can serve to reestablish lost self-esteem. It also lends itself to restructuring of time, which now can be more harmoniously geared to the realities of one's new daily life.

Persons who are inclined to let outside forces determine their life patterns, lean towards the other extreme. If there is no definite time regime they may not get up in the morning. They eat at irregular intervals and then only whatever is at hand. They may attend events if others urge them to do so, perhaps even escorting them there in person, but rarely by their own initiative. Many will drift into an existence that is characterized by boredom, lethargy, and stagnation. Some may arrive at a happy adjustment by relaxing and enjoying their freedom from inner and outer compulsions. They consider the time for the extension of energy as being past. They have done their share; they deserve their rest. To be sure, a certain degree of lassitude and placidity may take over. As interests are withdrawn from the outside they become directed more and more toward the self. However, these persons usually feel quite satisfied and do not wish for any changes. According to some authors, who have studied various adjustments to aging, this represents one of the three "good adjustments," frequently called the "Rocking Chair Type."[3]

(e) Perhaps the majority of these reactions can be compared to other withdrawal symptoms. Just as the physical organism which has become habituated to certain substances—desirable or undesirable—cannot overnight reestablish its balance when these substances are withheld, so the person as a whole cannot adjust to the absence of that to which he had become adjusted throughout his work life, without mobilizing his internal defenses or utilizing external resources.

Successful Adaptations

The most successful adaptation occurs when change takes place over an extended period of time, and continuity is preserved. This is enhanced, for instance, by the gradual reduction of work hours or modification of duties. The person who owns a family farm or small business can give up some of his responsibilities, provided others are willing to assume his duties. The same applies to professionals in private practice such as lawyers, dentists, and certainly physicians. Yet I wonder how many among the medical profession would select this option, or even consider it seriously. To this writer's knowledge there are no studies available that deal with this question. It seems to me though that only a minute fraction do choose this alternative and then, mainly for health reasons. On the other hand, I know of a few physicians who have been employed in various medical or teaching institutions and who, after mandatory retirement, secured part-time positions in the same or other institutional settings.

Other choices consist of offering one's professional skills on a voluntary basis. Physicians and other health professionals are in such demand, especially in many of the newer programs that provide for services to the disadvantaged, that there is no dearth of such opportunities. Further variations consist of starting earlier to use one's best professional know-how and wisdom in other than purely work or position related endeavors. Through this one establishes connections which will continue beyond retirement. In addition, because such activities are usually carried on in conjunction with the interest and involvement of other persons, they offer an excellent chance of replacing part of the lost companionship of one's former colleagues. Furthermore, one remains in touch with the field which had been of such vital importance in the life of most professionals.

Continuity can also be preserved by tapping other sources. Interest in fellow humans and in the humanities, talents and skills, hobbies and sports, all these outlets for one's creativity, if encouraged to develop through childhood and maturity offer opportunities to continue leading a fully occupied life. Retirement can become a period rich in new discoveries and in continued growth.

Although the mainsprings for such positive adaptations are located within the individual, environmental conditions must be conducive to the realization of these potentials. Many new programs have been recently designed to provide opportunities for activities and involvement for retired persons. Recreational and educational programs are offered by Senior Centers, colleges, churches, and many other community agencies. Volunteer programs on local or national scales are aimed at tapping the skills of retirees and their desire to be of help and to match them with the needs of others. Foster Grandparents and Retired Senior Volunteer Programs (RSVP) are just two of the better known voluntary programs. Organizations such as the American Association of Retired Persons (AARP) and the National Council of Senior Citizens (NCSC) and lately local federations, provide certain specific advantages to their members. They also attempt to bring about positive changes in public policy, private pension plans, and in other conditions through social action. Individuals who wish to actively participate in social action find excellent channels for working in the interests of older Americans. Valuable and indeed necessary as these programs are, they do not take the place of those which would lead to the instilling and nurturing of those indigenous interests and of qualities within individuals which make transition from work to retirement less painful, and which can lead to a more productive late period of life.

Unfortunately, so far many older members of our society are singularly ill-prepared for such continuities and for making use of the opportunities of the retirement period. In 1963, Dr. Martin stated that our exclusive work orientation diminishes our capacity for relaxation and that our efforts have become entirely outer directed and utilitarian.[4] In a recent publication, Gordon Dahl discusses the need for developing new attitudes designed to balance the emerging "leisure ethic" with the prevailing "work ethic." He believes that the main obstacle to this balancing can be found in our tendency to confuse work, play, and worship by: "Worshiping our work—working at play—and playing at worship."[5]

Differences in Adjustment

Several studies attempt to isolate factors related to good retirement adaptation. Life satisfaction shows positive relationship to social roles, pursuit of previously held interests or life-long wishes, and to anticipatory socialization.[6] The latter includes pre-retirement programs as conducted by some industries, and lately also by other institutions such as colleges, etc. Beneficial results are evident during the early stages of retirement, but differences usually disappear after three years. This does not speak against the program per se. Rather they may indicate that such programs should be available to all, that they should start earlier, and that they should include topics in addition to those which are of a practical and informational nature. It is further agreed that pre-retirement counseling should include the spouses of the prospective retiree.

So far, attention has focused almost entirely on male workers, with occasional inclusion of women in their roles of wives and their reactions to the husband's retirement.[7]

Another group of studies conducted by the Duke University Center for the Study of Aging and Human Development compares subjects and their wives from different educational and occupational levels.[8] A sample of 108 couples was divided into an upper educational stratum composed of managers and professionals, a middle layer consisting of clerical and sales personnel, and a lower level composed of craftsmen, industrial, and manual laborers. Attitudes of the two upper groups were rather similar, but differed sharply from those of the lower group. Among the most relevant findings were the following:

The upper educational group did not welcome the prospect of retirement, often expressing bitterness and disappointment about mandatory retirement. Their wives also held unfavorable expectations, though to a lesser degree. Nevertheless, both actively planned together for the immediate future. Shortly after retirement, most men found that it was far better than anticipated; their wives also showed a shift towards more positive attitudes. After five years, husbands' views of retirement became more disillusioned. Observation of the lowest occupational group showed a reversal of these trends. Men welcomed retirement, but were quickly disappointed, and to a higher degree. Their wives were less involved in planning and in making accommodations to the couples' changed circumstances; their views were, and remained, more negative. In all three groups, husbands after retirement, began to share with their wives in household chores. This participation was highest in the upper educational group, and furthermore, it led to less friction than in the lowest occupational level.

Based on these studies and on observation, one can expect that professionals are better prepared for retirement than other segments of the population. Perhaps they are quicker to adjust to changed circumstances and are better equipped to cope with stress; perhaps they find more support within their marriages and families. One can also assume that their financial situation is such that they do not feel the economic squeeze to the same extent. Also, they are more familiar with community resources and are better able to make use of them. Their life-long interests, and intellectual engagements, provide for the continuity and for the ongoing involvement in that which had given meaning to their lives before retirement. Furthermore, restructuring of time, through adjusting one's rhythm to that of the new daily life pattern, moving into new roles, establishing new relationships, gaining new insights, all can be within easy reach of the professional person who can make use of his strengths, abilities, and internal resources. All of these then, in turn, evolve into a new self-image with self-respect and awareness of purpose. Retirement is not free of stress; nor does it have to be a period of stagnation and futility. With positive adaptation we can make it a successful and gratifying stage of life.

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Cover Photo

"Stone Jewelry"

The Mexican Lace Agate used for the stone jewelry on this month's cover was obtained by Dr. F. A. Zinter in Rochester about three years ago, roughly a stone 5x5x4 inches, slabbed months later, the pendant portion cut out, shaped and polished, and the silver work completed in time for a Mothers Day presentation a year ago. Since then, a matching pair of earrings and a ring from the same stone have been completed. This was the only slab that had this particular design so there is no duplication of design!

In May of 1973, a 20-year certificate was awarded to Dr. Zinter by the Minneapolis Vocational Evening School to which another year has been added. Here most of the slabbing of large agates, preforming, rough grinding and sanding is done and the finishing is done at his home. The major portion of the jewelry making and hammering of hollow ware is done there since the noise level is quite high!

Photography had been the number one hobby of Dr. Zinter until silver smithing came about. Although he holds a few awards from the American Physicians Art Association, photography has been used mainly in photographing Minnesota wild flowers, the polished rocks, and finished products. Dr. Zinter is a general practitioner with offices in Minneapolis.

One Alternative to Institutionalization

In-Home Supportive Services

SHARON KAY PATTEN, MSW, ACSW*

During the last few years there has been increasing discussion in the public and private sectors on the quality of care being provided in institutions for the elderly. Expressions of this interest have come from sources ranging from the publications of the Special Committee on Aging of the United States Senate and the office of Ralph Nader to the actions of the Minnesota State Legislature. The economic factor continues to be of vital interest. Some recent figures show one of the reasons for this concern· In fiscal year 1973 an estimated total of about $3.2 billion, of which $1.4 billion were private monies and $1.8 billion were public monies, were expended for nursing home care for persons 65 years of age and older. Of this total of $1.8 billion, federal funds accounted for approximately $1.1 billion with the balance of $691 million coming from state and local sources. All other age groups spent a total of $425 million of public monies for nursing home care.[1]

The increase over the last decades in numbers of the elderly population has provided an impetus for action. According to the 1970 Census, there are approximately 20 million persons or about one-tenth of the population who are 65 years of age and over. Significantly, the oldest segment of the population over 65 is presently growing fastest with the median age having gradually risen to 73 years. Approximately eight million or four out of every 10 older Americans are 75+ and of these over one million are 85+.[2]

Today, approximately six percent of the aging are institutionalized which represents about one million persons. Estimates by the Census Bureau indicate that the elderly population will rise to 23.5 million in 1980 and 27.5 million in 1990.[3] The number of persons aged 65 or over will probably continue to increase through the next several decades. The percent in this group compared to the total population, however, may continue to increase but at a very decelerated rate.

With advancing age comes an increased likelihood of such problems as chronic illness, reduced income, decreased mobility, reduced energy level, and social isolation. As the total number of persons in the oldest segment of the population increases in the coming years, there will be an increase in the demand (latent or expressed) for various in-home supportive services such as transportation, homemaker services, chore services, meal preparation, and nursing services.

Recent discussion has centered not only on the quality of care and on related costs, but also on the feasibility of various alternatives and service options to institutional care for the aging. The need for institutional care for a small segment of the elderly population should be recognized, but recent information and data indicate that a significant percent of the institutionalized elderly population could live at a lower level of service care, such as in their own place of residence. Many of these persons would need a combination of in-home supportive services.

Research on Alternatives

A limited amount of research has been conducted to explore possible alternatives and options to institutional care (which generally means in a nursing home). There is little data on projected costs, on needed changes in delivery systems, on characteristics of the population to be served, and on financing mechanisms for these various options. The actual parameters on both the demand and supply sides are not known. A hypothesis underlying some of the work in this area is that there are residents in institutions who could be maintained at home if various supportive services were available and accessible to them.

The four studies referred to here were conducted in Massachusetts,[4] Florida,[5] New York,[6] and Minnesota.[7] The last study was conducted by the author in Hennepin County during the spring of 1972. These studies indicate that "inappropriate" placement of elderly in nursing homes does occur and that:

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1. A range of 16 to 63 percent of elderly nursing home residents do not require the level of care and services they are presently receiving. A significant percent of nursing home residents could manage at a lower level of care. There are indications that some residents need more intensive care than is presently being provided.
2. A range of 10 to 30 percent of elderly nursing home residents could be maintained in the community. Many of these persons would need, however, a combination of in-home supportive services; and
3. According to the Florida study, most older persons prefer to reside in their own home than in an institutional setting.

Over-Utilization of Nursing Homes

There are many reasons for over-utilization of nursing home care. A necessary, if not sufficient condition, is the paucity of viable alternatives in the community.

The present supply of supportive services that could help some older persons manage in the home is limited. Those services that are available are directed at acute, short-term problems, thus lending little support to the chronic conditions prevalent with advancing age.

There exists a general inability of the social service and health delivery systems to address the multiple needs of older persons. An older person may need a combination of two or more services such as transportation, meals, home nursing, and chore services. Another troublesome area is the lack of coordination between or within providers of service.

Accompanying this is the present inability of the system to adjust to the changing needs of its clients. The combination and quantity (number of units) of services required will likely change over time. Too often the system is not sufficiently flexible to respond in a timely and supportive way.

A barrier to the creation of alternatives is the acceptance by the general public that when an older individual approaches a marginal existence in the community, the next "logical" step is to the nursing home.

Presently, financial mechanisms to pay for alternatives are inadequate to meet the needs of older persons who live on low or moderate incomes.

It is difficult to predict the cost differentials between institutional care and a program of in-home supportive services or any other service care option. There is a dearth of data and information on these services and on the characteristics of the population served or requiring such services. The specification of data items is at a beginning stage and lacks uniformity across agencies. It is almost certain that the latent demand for in-home supportive services greatly exceeds the present supply.

A related problem is the difficult, frustrating, and time consuming task of attempting to obtain needed in-home supportive services. Financial and psychological resources of families and friends are often drained before any significant intervention occurs. The point of intervention is usually late and under crises conditions. The end result is often a one way move to a nursing home, whether or not this is the appropriate placement.

It is not only the potential consumer and related persons who fail to have adequate information. A host of professionals, including doctors and social workers, frequently do not have ready access to information on existing resources. Related to the above is often the lack of a community resource where potential consumers and related individuals can discuss with social workers and other appropriate professionals the problems confronting them.

Difficulties in Deriving Estimates

Numerous problems arise when estimates are being derived. The following list outlines several major problem areas:

1. Uniform, usable data is not systematically collected by the various providers of in-home supportive services.
2. The available data provides few clues to the characteristics of the population now receiving services—family composition, age, income level, type of residence, race, sex, type of disability, etc.
3. There is little information on the characteristics of the population in nursing homes and in other institutions.
4. There is need for detailed information on the volume and the types of services presently provided.

5. Available data provides few clues to the varied combination(s) of services required; the volume of units of services required or the definition of a unit of service.
6. The information available on the expressed demand is miniscule, but data on the demand which has gone unmet and on the latent demand is almost non-existent.

To attempt to derive at population, cost, demand and supply estimates under these circumstances is a difficult task. With these problems in mind, I drafted some preliminary estimates, some of which are provided in the following sections. The Table provides estimates on the number of non-institutionalized elderly in Hennepin County who might make use of in-home supportive services based on 1970 population figures.

The estimates are derived in a manner similar to the national estimates by Dr. Robert Morris and associates at Brandeis University.[9] As indicated on the table, several statistical sources were utilized in developing these estimates with the major source being the National Health Survey of the Public Health Service.

Estimate No. 1 is derived from national statistics on mobility and chronic conditions of the elderly population. Limitation of mobility refers to a person's ability to move freely. Estimate No. 2 is derived from similar statistics on the ability to carry on a major activity. Limitation of activity refers to the major activity of the individual such as ability to work or keep house as well as his or her ability to participate in recreational, civic, or church activities.

According to these two estimates, between approximately 9,500 and 11,800 non-institutionalized persons 65+ were likely candidates for in-home supportive services in Hennepin County in 1970.

I have also attempted to derive estimates on the elderly residing in nursing homes in Hennepin County who could manage at home. Estimates range from about 600 to over 1,800 elderly persons in Hennepin County nursing homes who could manage at home. Many of these persons would require a combination of in-home supportive services.

Another estimate that is very difficult to get at is the cost differential between a program of in-home supportive services and services provided in an institutional setting such as in a nursing home. By employing some of the findings from the study in Hennepin County, some "ball park" figures were drafted. In summary, data from the hypothetical case which was developed do not indicate lower financial costs for the maintenance of an elderly person in his own home, as opposed to care in an institutional setting. Great caution, however, must be given when interpreting these results, since there is not sufficient information to calculate with certainty the cost differentials.

Discussion

The preceding paragraphs touched on some major points of my Plan B paper in Public Affairs on

TABLE
The Non-Institutionalized Elderly in Hennepin County Who Might Utilize In-Home Supportive Services (1970)*[8]

	Both Sexes	Male	Female
Total Elderly, 1970	93,002	35,779	57,223
Living in institution	7,354	2,451	4,903
Living in non-institutional setting	85,648	33,328	52,320
With no chronic conditions	12,333	5,199	7,063
With 1 chronic condition or more	73,315	28,129	45,257
With no limitation in mobility	57,299	22,263	35,002
With some limitations in mobility	16,016	5,866	10,255
Has trouble getting around	6,595	2,466	4,133
Needs help in getting around	5,396	2,033	3,401
Confined to the house	4,111	1,366	2,773
Total needing help or confined to the house	9,507	3,399	6,174
Estimate No. 1 of eligible elderly population	9,507	3,399	6,174
Population 65 years and older unable to carry on major activity			11,819
Estimate No. 2 of eligible elderly persons			11,819

*Estimate by Sharon Patten based on extrapolations from National Health Survey, Vital and Health Statistics, U.S. Department of Health, Education and Welfare, Public Health Service, HSMHA and from data from the 1970 Census. Since on a national basis women outnumber men two to one in institutions, this ratio was utilized in the above estimates. The unevenness in the totals and subtotals of columns and rows is due to the "rounding off" process.

in-home supportive services as one alternative to institutionalization. In that paper, I recommended the development of a large scale experimental project of in-home supportive services in an urban and rural setting. Some suggested parameters were delineated in the paper. A second recommendation was that the project be preceded by a detailed study to design the project and the evaluation.

In an attempt to further explore the area of alternatives and service options for the aging, the Minnesota Governor's Citizens Council on Aging let a contract for this planning study to the School of Public Affairs, the University of Minnesota with Dr. Nancy N. Anderson as the principal investigator·

The study involves the following three major tasks: (1) the analysis of alternative arrangements for the provision of services to older persons with particular focus on the demand for these services, the available or potential supply of such services, and the barriers to more public support of non-institutional maintenance of older persons; (2) an analysis of comparative costs of nursing home services, out-patient services, and in-home supportive services to the extent accessible data allow; and (3) the design of an experimental project to provide services to persons outside of nursing homes and to evaluate the costs and benefits.

It is anticipated that this initial planning effort by the Governor's Citizens Council on Aging and the School of Public Affairs will lead to the development of a large scale services project to compare institutional care with alternative service options for specific target populations. Only as information and data are carefully gathered, analyzed and utilized within a policy and program framework, will decision-making become less muddy and more informed.

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This brand she quenched in a cool well by,
Which from Love's fire took heat perpetual,
Growing a bath and healthful remedy
For men diseased; but I, my mistress' thrall,
    Came there for cure, and this by that I prove,
    *Love's fire heats water, water cools not love.**

---

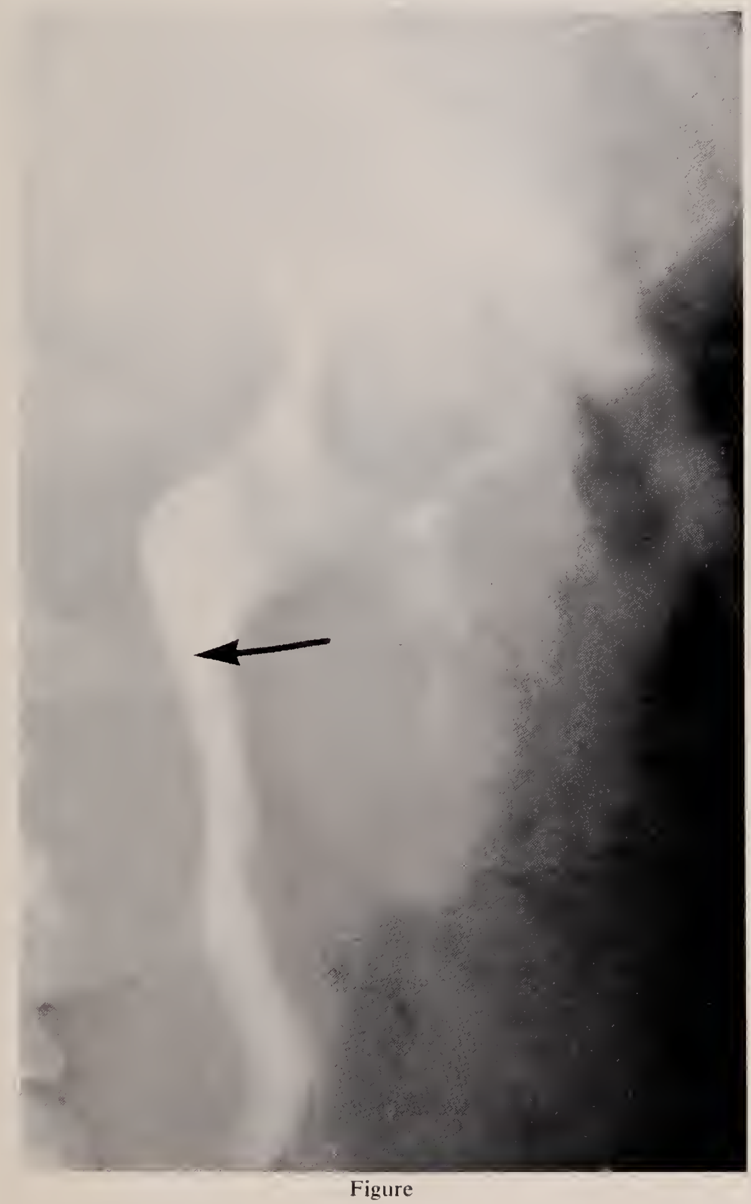
*Shakespeare: Sonnets, CLIV.

White Chunks in the Urine

A 31-year-old woman was admitted after noticing the passage of chunks of white material in the urine. There was a past history of repeated episodes of urinary stones. Physical examination and routine blood studies were normal. Urinalysis was normal except for albumin and occasional red cells. Urine cultures were sterile.

Excretory urography was done (Figure) and disclosed an isolated, flat, plaque-like filling defect with a furrowed surface (arrow) in the left renal pelvis at its junction with the ureter.

What is your diagnosis? (See next page.)



Figure

Diagnosis: Leukoplakia of the left renal pelvis.

Leukoplakia of the renal pelvis or renal cholesteatoma is a metaplasia of the transitional epithelium towards the squamous side with keratinization. It is a rare disease with malignant potential and occurs in middle age patients with no sex preference. The reported incidence of bilateral involvement is 10%. However, six out of the nine cases documented by Smith, Webb and Price[3] were marked by bilaterality. The usual history is that of recurrent episodes of urinary infections with chills, fever, renal colic and bladder irritation over a period of many years. Hematuria occurs in about one third of the patients. Passage of desquamated squamous cells in the form of gritty flakes, soft stones, white chunks, or membrane or tissue with the urine is considered to be of diagnostic significance. The prognosis is that of a progressive disease leading eventually to destruction of the kidney.

On urograms and pyelograms the lesion, when large enough, may be seen in the renal pelvis and calyces as single or multiple, scattered or confluent plaque-like filling defects with a striated, wrinkled, furrowed or layered appearance (Figure, arrow). Piling up or detachment of the keratin produces other filling defects that simulate tumors or stones in the pelviocalyceal system and the ureter. Hydroureter, hydronephrosis, pyonephrosis and ultimate renal failure are the sequalae of obstruction and infection. Neoplasms, stones and inflammatory processes including tuberculosis should be considered in the differential diagnosis.

Treatment is reported to be generally unsatisfactory. Nephrectomy is usually performed in unilateral cases. Conservative management is aimed at preservation of functioning nephrons.

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Hennepin County General Hospital
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Meeting

Northwestern Pediatric Society

The fall meeting of the Northwestern Pediatric Society will meet on Friday, September 20, 1974 at the Chanhassen Frontier, Chanhassen, Minnesota.

There will be presentations of original papers and the guest speaker will be Joseph A. Bellanti, M.D. Professor of Pediatrics and Microbiology, Georgetown University School of Medicine, Washington, D.C.

For further information, contact R. James Vaccarella, M.D., Secretary-Treasurer, Northwestern Pedatric Society, 565 Snelling Avenue South, St. Paul, Minnesota 55116.

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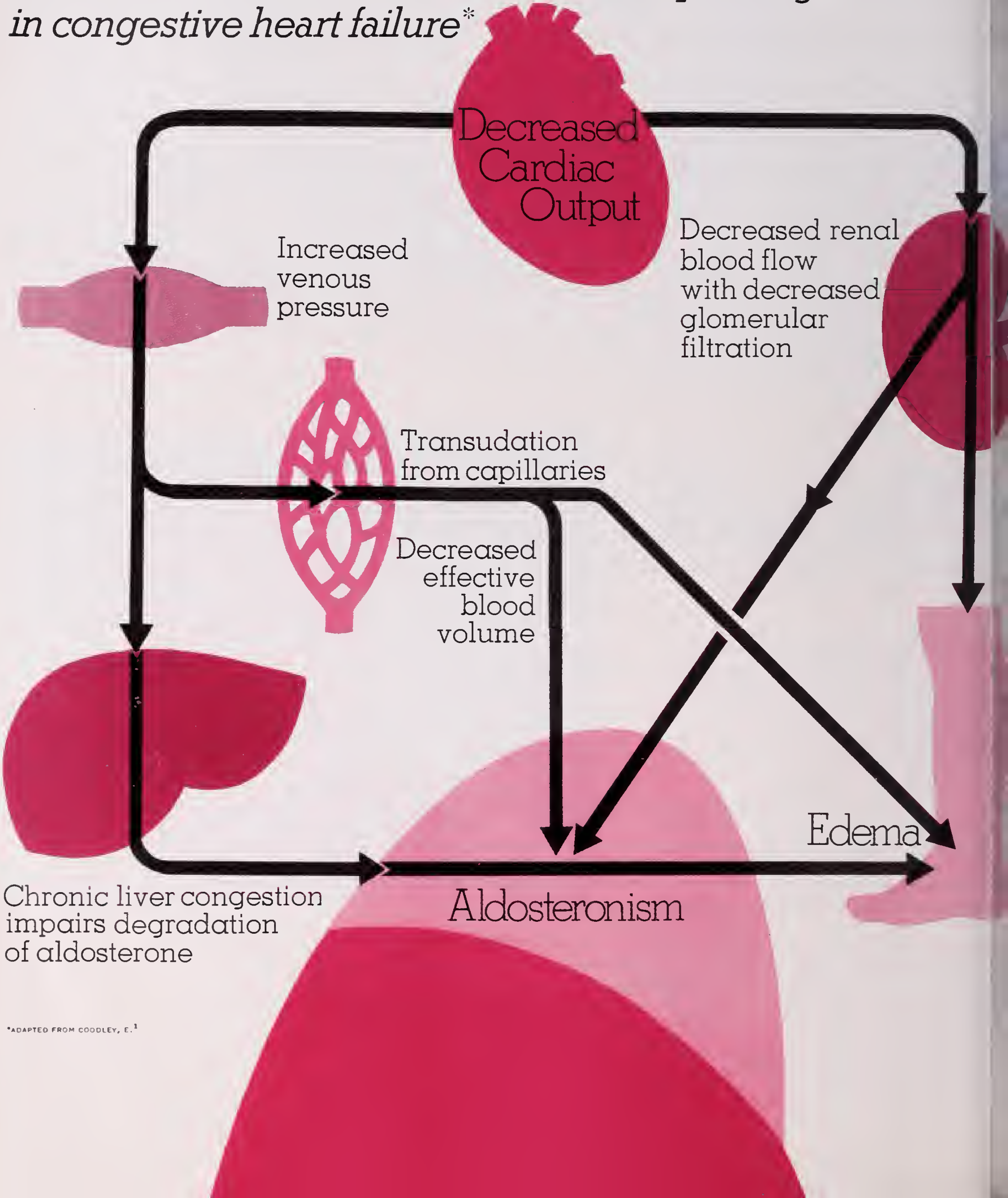
Decreased Cardiac Output
Increased venous pressure
Decreased renal blood flow with decreased glomerular filtration
Transudation from capillaries
Decreased effective blood volume
Edema
Aldosteronism
Chronic liver congestion impairs degradation of aldosterone

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nimizes potassium deficiency and
tentiates effect of "add-on" diuretic.[2]
Avoids acute volume depletion and
dosterone rebound.[2]

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laily dose of a thiazide
Permits daily additive diuretic effect
ile maintaining potassium balance.

Indications—Essential hypertension; edema or ascites of congestive heart failure, cirrhosis of the liver and the nephrotic syndrome; idiopathic edema Some patients with malignant effusions may benefit from Aldactone (spironolactone), particularly when given with a thiazide diuretic

Contraindications—Acute renal insufficiency, rapidly progressing impairment of renal function, anuria and hyperkalemia.

Warnings—Potassium supplementation may cause hyperkalemia and is not indicated unless a glucocorticoid is also given. Discontinue potassium supplementation if hyperkalemia develops. **Usage of any drug in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the mother and fetus.**

Precautions—Patients should be checked carefully since electrolyte imbalance may occur. Although usually insignificant, hyperkalemia may be serious when renal impairment exists; deaths have occurred. Hyponatremia, manifested by dryness of the mouth, thirst, lethargy and drowsiness, together with a low serum sodium may be caused or aggravated, especially when Aldactone is combined with other diuretics Elevation of BUN may occur, especially when pretreatment hyperazotemia exists. Mild acidosis may occur. Reduce the dosage of other antihypertensive drugs, particularly the ganglionic blocking agents, by at least 50 percent when adding Aldactone since it may potentiate their action.

Adverse Reactions—Drowsiness, lethargy, headache, diarrhea and other gastrointestinal symptoms, maculopapular or erythematous cutaneous eruptions, urticaria, mental confusion, drug fever, ataxia, gynecomastia, inability to achieve or maintain erection, mild androgenic effects, including hirsutism, irregular menses and deepening voice. Adverse reactions are infrequent and usually reversible.

Dosage and Administration—For **essential hypertension** in **adults** the daily dosage is 50 to 100 mg. in divided doses. Aldactone may be combined with a thiazide diuretic if necessary. Continue treatment for two weeks or longer since an adequate response may not occur sooner. Adjust subsequent dosage according to response of patient.

For edema, ascites or **effusions** in **adults** initial daily dosage is 100 mg. in divided doses. Continue medication for at least five days to determine diuretic response; add a thiazide or organic mercurial if adequate diuretic response has not occurred. Aldactone dosage should not be changed when other therapy is added. A daily dosage of Aldactone considerably greater than 75 mg may be given if necessary.

A glucocorticoid, such as 15 to 20 mg. of prednisone daily, may be desirable for patients with extremely resistant edema which does not respond adequately to Aldactone and a conventional diuretic. Observe the usual precautions applicable to glucocorticoid therapy; supplemental potassium will usually be necessary. Such patients frequently have an associated hyponatremia—restriction of fluid intake to 1 liter per day or administration of mannitol or urea may be necessary (these measures are contraindicated in patients with uremia or severely impaired renal function). Mannitol is contraindicated in patients with congestive heart failure, and urea is contraindicated with a history or signs of hepatic coma unless the patient is receiving antibiotics orally to "sterilize" the gastrointestinal tract.

Glucocorticoids should probably be given first to patients with nephrosis since Aldactone, although useful for diuresis, will not directly affect the basic pathologic process.

For **children** the daily dosage should provide 1.5 mg of Aldactone per pound of body weight

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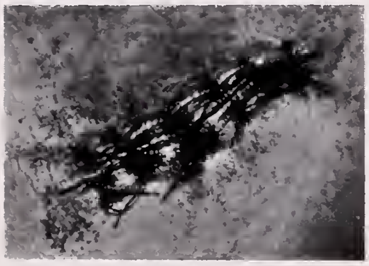

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Editorials

Does Psychiatry Neglect the Aged?

NEGLECT IS A WORD with unpleasant connotaions and may possibly be an inappropriate word n this context. Yet we cannot ignore the striking data that only two to three percent of the patients seen in various psychiatric clinics and Mental Health Centers are over 65 years of age; this is clearly an under representation when we consider hat ten percent of the population are over 65 and that in this age group psychologic disturbance s more frequent than in younger age groups.

How do we explain this under utilization of outpatient psychiatric facilities by older people? In part, it occurs because the older people of today grew up at a time when psychiatrists were mostly hospital neuropsychiatrists who took care of "crazy people"; therefore today's elderly do not ordinarily think of themselves as needing a psychiatrist nor do they consider that their problems an be helped by a psychiatrist. A further partial xplanation of under utilization is that first line practitioners and professionals such as physicians, ministers, nurses, and social workers often do not ecognize psychologic disturbance as such in the lderly and if they do recognize it they may not be ware of what psychiatry has to offer.

But what part do psychiatrists themselves play n the under utilization of psychiatric facilities by lder people? This question suggests several others hat may lead us to some understanding of the roblem. Are psychologic problems in the elderly reatable? The answer is a resounding YES. All oo often psychologic disturbance in the aged is thought of in terms of Senile Dementia or Cerebral Ateriosclerosis for which treatment is limited; yet these conditions represent an important but small percentage of patients who need help. Depression, anxiety, somatization, social alienation, and such make up the bulk of the problems of the elderly and are eminently treatable on an outpatient basis with various psychotherapies, social therapies, pharmacologic treatments as well as various interventions with the family and the community.

Are older patients gratifying for the psychiatrist? I wish the answer to this question could be an equally resounding YES but the fact of the matter is that it depends on the psychiatrist. Some of us suffer from gerontophobia and approach older patients with anxiety or do not approach them at all because we are reminded by them that we too are aging. But for many, the elderly are beautiful as people and as patients; they respond well to treatment and are greatly appreciative of what is done for them. Hopefully, more and more of us will be able to learn to enjoy treating the elderly.

Is treating the older patient an efficient use of professional time? Psychiatrists are not able to meet society's needs for treatment of mental and emotional problems and they must reasonably ask if the amount of time they spend can be justified in terms of probable outcome of treatment and of long term prognosis. Since older patients, reason some, have a relatively short life expectancy, a psychiatrist is not justified in spending many hours, as for example, in psychotherapy with an older patient. This reasoning, seems to me, is fallacious both from a humanistic point of view and a cost benefit point of view. Older people do deserve our time. Clinical experience clearly demonstrates that timely intervention in the treatment of the aged can prevent costly hospitalization and institutionalization and reduces disruption in the extended family of the older patient. Further, Medicine has prolonged life and therefore Medicine is obligate to use its skills and knowledge to improve th quality of that prolonged life. Certainly reductio of mental and emotional anguish would contribut greatly to the quality of life of the aged. It is m hope that the articles in this special issue of MINNESOTA MEDICINE will help all practitioners o medicine to add to that quality of life in the aged

Floyd B. Garetz, M.D
Guest Edito

The Doctor's Role in the Nursing Home

THE NURSING HOME industry presently is struggling for an identity in the health care field and desperately needs input from practicing physicians at the local level. A nursing coordinator in a large metropolitan nursing home laid this indictment at the door of the medical profession. "The uninterested and apathetic physicians that enter my nursing home have a devastating effect on the morale of the patients, nurses, nurse's aides, occupational therapists, housekeeping and dietary staffs." Reflecting on this, I reviewed the physicians attending the course on human aging presented by the University of Minnesota on March 28 and 30, 1974. There were 24 men on the faculty presenting the course. There were eight physicians registered from the State of Minnesota. In gathering material for this paper, the author could not find one current periodical on aging in a 500 bed hospital library that prizes itself on having publications of 250 periodicals. In my opinion this apathy results from the frustrations physicians feel with the magnitude of their responsibility in rehabilitating the elderly disabled, from the poor psychological and philosophical preparation of physicians for their role in caring for the disabled and from the lack of definition of the physician's role. As a result, the doctor provides episodic emergency care which disrupts his regular office hours and his leisure time and at times demands almost heroic measures in order to deliver the proper care to a near catastrophe. With this paper I hope to present to physicians a role that will reward time and effort, will prevent many emergencies, will give better total patient care and will bring the nursing homes into closer ties with our established delivery care system.

Society, through its governing bodies, has state that the physician will take an active role in carin for the elderly. Physicians must order therapy an drugs. They must document the level of care patient is to receive. Physicians must see patient at regular intervals. A recent letter dated Marc 28, 1974, from the Hennepin County Welfare Department stated that it will be the facility's responsibility to see that physicians visit their patient at designated intervals. Since most nursing home receive about 70 percent of their funds from th Welfare Department and since the Welfare Department is placing the responsibility for the regular visitation of the patients by the doctor with th institution, the inevitable is obvious. The financia stability of the nursing home will be in jeopard if it is unable to gain the cooperation of the physician whose patients reside in its home. It is m earnest hope that physicians in private practic will assume a more active role in the nursing hom industry. If they do not, the nursing homes wil be forced to hire physicians to insure complianc with Welfare directives. With this loss of fre choice of physician, I see a clean breakaway fror our traditional delivery of medical care.

Before outlining the physician's role, I woul like you to reflect momentarily on our yout oriented culture. Following this, I would lik you to reflect briefly on the attitudes of differer people involved in the decision to place a perso in a nursing home.

First and foremost is the attitude of the physician toward the nursing home; secondly, the feelings of the patient who has been gradually aging losing identity, losing his or her ability to d practical work; thirdly, the attitudes and feeling of the family of the patient who may feel they are abandoning their loved one to a nursing home; and then the attitude of the staff of the nursing home who may receive little support from the physician, hostility from the patient and blame from the patient's family. In this group whose opinion is most sought after and most respected? Who can give support, understanding and encouragement to all? Obviously the physician is the cornerstone. In order for the physician to do this he must examine and understand his own feelings and attitudes toward disease and toward death. It occurs to me that we physicians have been trained to make sophisticated diagnoses and administer appropriate therapy. The goal of this training is to cure the patient's illness. When confronted with a disease that we cannot cure, we have not been taught our role of support, our role as an equal collaborator with the patient, our role of encouragement to the patient, our role of support to the relatives, our role of encouragement and support to the staff who must deal daily with a patient they know has no hope of cure. Do physicians understand how important and difficult it is to maintain the morale of a nursing home staff who daily must support the many extremely ill and debilitated patient?

Reflecting on this, I suppose the first role of the physician would be that of an encouraging and supporting confidant. It is not unusual for the patient or the family to lash out at the delivery care system because of discouragement or guilt feelings and the physician must understand these feelings to be able to deal with them appropriately. In this role the physician has an independent opinion. The physician doesn't pay the bill, however his signature has the power and responsibility to deliver occupational therapy, physiotherapy, special diets, drugs and other treatment to the patient. The patient and the family know this. With his medical knowledge he can assure good care by the nursing home and still protect the staff from unreasonable demands by patients and relatives.

The second role of the physician is easily identified as the traditional role of the physician to the patient. The question here is how to deliver this care. Dr. Bennett Gurian* states that when his department initially became involved in the care of the elderly in Boston, they offered to cover some of the Boston nursing homes for emergencies in patients who had no attending physician, or for patients whose attending physician would not respond. The demand for this service was so overwhelming that the Department was unable to cope with the situation. Therefore, they inaugurated a system of regularly scheduled visits to the nursing home. Immediately emergency calls were practically eliminated. My experience parallels Dr. Gurian's. Regularly scheduled nursing home rounds result in more efficient use of the physician's time by reducing the number of telephone contacts and emergency visits. These rounds give the patient a tremendous psychological boost and gives the staff an identifiable leader. In this role the physician will find it necessary to seek out literature and continuation courses that deal with the older patient. The medical characteristics of the elderly relating to drug dosage and drug complications are well documented. The physician's role will be much easier if the doctor will share his responsibility with the patient, the family and staff. A physician who can see his role as an equal collaborator will force all involved to have a stake in the success of rehabilitation and the quality of the patient's life. Nursing care conferences and family conferences are helpful in clarifying goals for all interested in the patient. The physician need not attend these conferences. However, the conferences need his input through the nursing staff and his interest in and support of the goals of his patient's care.

The third role of the physician as a teacher will help develop nursing procedures and patient care policies. Routine nursing procedures thus developed can be quickly and easily taught to new staff so that a consistent level of care is maintained. All of these routines are aimed at preventing disease progression and eliminating emergencies.

Again the physician is an equal collaborator with the staff in developing routine care policies and procedures, thus giving the staff a stake in its success. To develop routines the physician may find it necessary to obtain expert opinions from his contacts in the hospital community, i.e., urologist for catheter care, fire marshal for fire drills, dietitian for special diets, orthopods for routine hip care, etc. Without the active participation of a local physician, nursing homes find it most difficult to obtain this type of input. The input by a physician doesn't always need to be a formal meeting. Informal conversation with the nursing supervisor or nursing home administrators often is sufficient. Regular in service nursing education provides a means for input from all the resources at the physician's disposal. The subjects covered and type of instructors used are a good index to the type of care available in a nursing home.

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*Director of the Department of Geriatrics, Massachusetts General Health Center in Boston.

Every nursing home has a personality and this personality reflects the background, education, values and goals of the administration. The physician teacher has a responsibility to help mold this personality and in this way influence the psychological and psychosocial rehabilitation of the patient. The physician will be least prepared in this role. He can gain help from the Psychology Department of the University of Minnesota and the Veterans Administration, as well as independent organizations such as the Alfred Adler Institute of Minnesota. In my opinion the physician can influence the whole nursing home community by his respect for individuals, whether patient or staff, by encouraging self respect by responsibility, by recognizing a disability need not be a handicap, and by identifying goals of patient behavior to aid the staff in behavioral modification.

Medical directors and the utilization review committee men are formal titles for physicians who are active in nursing home care. I would expect these physicians to fill all the roles I have mentioned, yet carry more responsibility in specific areas.

Our whole culture is undergoing a rather agonizing review of our attitudes toward life, illness and death. Society is asking the physician to lead in the development of adequate care of the elderly. Who is better able to do this than an interested physician who is willing to spend a few extra hours at continuation courses or in studying appropriate periodicals. I see the nursing home industry as an integral part of our delivery care system. The nursing homes are in need of massive input by clinicians in the private practice of medicine at the local level. The physician who will identify his or her role will facilitate this input. In my opinion the physician has a role as an understanding friend who gives encouragement and support, as a knowledgeable physician who will regularly attend the patient and feels comfortable as an equal collaborator with the patient and staff, and as a teacher who will readily share his expertise in developing and teaching patient care.

J. J. Pattee, M.D.
Minneapolis, Minnesota

Common Psychiatric Syndromes of the Aged

WE, AS PHYSICIANS, are all somewhat familiar with the aging process and some of the problems faced by the elderly. Many of us have wrestled with the disturbances presented by the aging person as he tries to cope with his environment with ever-decreasing resources and capabilities. Dr. Garetz'* scholarly presentation gives us a frame of reference in dealing with some of these problems.

Care and treatment deserve special emphasis. There is every reason to be optimistic and positive in dealing with these problems. With judicious use of ataractics and antidepressants (particularly the tricyclics), many of the depressions seen in the elderly can be treated on an outpatient basis. ECT† is very effective in depressions of the elderly and is especially useful when tricyclics are risky or contraindicated.

As the elderly develop senile and arteriosclerotic changes their ability to cope is markedly reduced and most of these people eventually require institutional care. Even here much can be done to ease agitation and gain their cooperation, by the use of modern drugs, but especially by understanding care rendered by a trained and sensitive staff. When shown such interest and concern the confused patient, able to maintain his dignity, often responds by being more comfortable, more cooperative, much less anxious and fearful.

J. C. L. Peteler, M.D.
Minneapolis, Minnesota

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*See page 618.
†Electric convulsive therapy.

Letters to the Editor

Dear Editor:

The recent report by Merrill, Markland, and Fraley[1] discussing a method of office urine bacteriology presents the reader with an interesting combination of oversimplification, error and compromised medical care. Comparison was made between a commercial urine culture and sensitivity kit used in an out-patient setting and urine culture in a hospital laboratory.

The commercial culture kit identified incorrectly one-third of the positive cultures. Is this inability a result of inherent deficiency in the kit or more likely due to a poorly trained technician, unschooled in the science of bacteriology? The described method of performing sensitivity testing is archaic. Since the monumental work of Bauer, Kirby, Sherris and Turck[2] on antibiotic susceptibility testing, the "zone or no-zone" method has been discredited. The FDA and the World Health Organization have officially endorsed Kirby-Bauer testing. The latter controls inoculum size, prescribes specific antibiotic discs and defines zones of inhibition that correlate well both with minimal inhibitory concentrations of antibiotic and in vivo therapeutic response. Erroneous answers result from the described technique. The belief that concentration of antibiotics in urine makes blood levels unimportant is incorrect; renal tissue antibiotic levels are essential for cure and are related to blood levels—not urine.

The advantages of the commercial kit are presented in terms of cost, time and convenience. With ordinary arithmetic, not including cost of sensitivity discs, labor, overhead, etc., the cost of one complete test is $4.15. Any laboratory test with such a high reagent expense costs four times as much, since reagents are between 10-25% of the cost of doing laboratory work. Is 48 hours an unreasonable interval of time to obtain a complete culture and sensitivity report? The authors' procedure requires 48 hours, assuming of course, that their technician wasn't doing part of the test at 2 a.m. As far as convenience to the physician or patient is concerned, patients are willing to accept a little inconvience to the alternative of unreliable laboratory testing; presuming, of course, that the patient is given the choice.

A glaring error in the report is the statement that "test standardization probably is of less importance in an office setting where a single technician consistently performs the same procedure than it is in a large laboratory with changing personnel." If the authors are correct, then dozens of reports from 1947[3] on, including scientific papers, data from the Center for Disease Control in Atlanta,[4] and our own Minnesota Department of Health[5] are wrong. The truth is that high laboratory proficiency exists in the larger hospital laboratories and that substandard laboratory work is frequently found in physicians' offices or small hospitals.

Our major objection to the report is the relegation of the science of bacteriology, a discipline requiring intensive education and experience, to a position where any untrained high school graduate with a 30 minute orientation could do equivalent work. Organism identification and sensitivity testing requires regular quality control of media, conditions and sensitivity discs. Good laboratories frequently detect problems; without quality control, the laboratory comfortably places its head in the sand, not knowing that trouble exists. Quality control is not a luxury, and quality control costs money. We deplore the anti-intellectualism in the report, where the tyranny of oversimplification is used to conceal ignorance. Laboratory work performed on this level cannot help but contribute to compromised medical care. Patients would be better served if the authors spent their time in clinical urology and left sophisticated laboratory tests to those more interested and better trained in laboratory medicine.

Seymour Handler, M.D.*
North Memorial Hospital

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*Assistant Professor, Department of Laboratory Medicine and Pathology, University of Minnesota, Pathologist, North Memorial Hospital, Minneapolis.

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1. Merrill DC, Markland C and Fraley EE: Office bacteriology. Minnesota Med 57:89, 1974.
2. Bauer, AW, Kirby WMM, Sherris SC and Turck M: Antibiotic susceptibility testing by a standardized single disc method. Amer J Cl Path 45:493, 1966.
3. Belk WP and Sunderman FW: A survey of the accuracy of clinical analysis in clinical laboratories. Am J Cl Path 17:853, 1947.
4. Finkel PW and Miller TR: A proficiency test assessment of clinical laboratory capability in the United States—National Bureau of Standards, Dept., HEW, May, 1973.
5. Merritt BR, McHugh RB, Kimball AC and Bauer H: A two-year study of clinical chemistry determinators in Minnesota Hospitals. Minnesota Med 48:939, 1965.

Dear Editor:

Dr. Handler's criticism is not entirely unexpected since our paper questions the necessity of referring all urine samples to a hospital or clinical laboratory for processing. This alternative to routine laboratory procedure, of course, has economic as well as medical implications.

Handler questions the accuracy of the "zone-no zone method" of determining antibiotic sensitivity testing stating that the FDA and World Health organizations have endorsed the Kirby-Bauer method. Apparently he would have us conclude that because these prestigious organizations recommend the Kirby-Bauer procedure, all other bacterial procedures have no place in clinical medicine. We do not accept this conclusion first, because based upon their recent track record, the FDA and World Health organizations are not infallible and second, because our study has shown that the "zone-no zone" technique is an accurate method to determine antibiotic sensitivity. Furthermore we would like to emphasize that the error induced by the "zone-no zone" method concerns the degree of sensitivity to the antibiotic being tested. Thus, by employing the "zone-no zone" method a physician may choose the second or third best antibiotic rather than the antibiotic to which the organism is most sensitive. As McLinn[1] suggests, this distinction is probably of more theoretical than practical significance in the treatment of urinary tract infections encountered in outpatients. This assumption was based on the fact that he found that only 1% of over 14,000 consecutive office cultures failed to respond to the drug indicated by the "zone-no zone" method.

Dr. Handler also questions the importance of antibiotic urine concentrations stating that "renal tissue levels are essential for cure and related to blood levels and not urine levels." On the contrary, the vast majority of outpatient urinary tract infections are confined to the bladder wherein urine concentrations are of primary importance. The significance of serum levels in urinary tract infections other than cystitis, for example in chronic pyelonephritis, is in our opinion questionable since chronic parenchymal infections seldom respond to medical treatment regardless of the antibiotic prescribed.

Three other comments by Handler require comment. First, the cost of materials is approximately $1.75, not $4.15 as he suggests. (Bacti-Lab plate 65¢ per test, Mueller-Hinton plate 75¢; and sensitivity disc 35¢). Second, our procedure requires only 24 hours, not 48 as he states, since the urines of all patients who have symptoms suggesting infection or microscopic pyuria are processed for antibiotic sensitivity testing as well as colony counts immediately. Thus, the results may be evaluated in 24 hours or less. Only those patients who are asymptomatic without microscopic pyuria may require 48 hours for a complete report of colony count and an antibody sensitivity. In the latter instance office bacteriology is primarily a screening method to discover patients with unsuspected urinary tract infections. Finally, we recognize the necessity for quality control; however, since the tests described are so simple to perform we do not believe that office bacteriology should be discarded simply because vigorous quality control is not available. Should routine urinalysis be eliminated from office practice also?

We presented the results of a study which indicated that urine cultures and antibiotic sensitivity testing could be performed accurately (96% and 95% correlation with hospital laboratory respectively) and economically in an office setting. Office bacteriology was not employed in this study, and is not indicated, in hospitalized patients presenting with life threatening bacterial infections wherein the choice of antibiotic is critical. On the other hand we believe that office bacteriology may be quite beneficial to practicing physicians, especially if they are located in rural areas where more sophisticated laboratory facilities are not readily available.

Daniel C. Merrill, M.D.
Minneapolis, Minnesota

Reference

1. McLinn PH and Tavel FR: Urine culture and drug disc sensitivity testing: A rapid, simple method for use in the office. Urol Digest 10:24, 1971.

Dear Editor:

The implications of Dr. Hilgers' article* and Dr. Carrier's accompanying editorial† are clear. Should the compulsory pregnancy forces ever win their battle and amend the constitution so as to forbid abortions, intrauterine devices would also be declared illegal.

Every physician who inserts intrauterine devices should inform his patients that they may be abortifacients and that they could be considered an outlaw for carrying one in their uterus if abortion is again made illegal.

Daniel Nussbaum, M.D.
Donald S. Lehman, M.D.

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*Hilgers, DW: Intrauterine Device—Contraceptive or Abortifacient? Minnesota Med 57:493, 1974.
†Carrier, Thomas C: Intrauterine Device, Minnesota Med 57:477, 1974.

O. L. Norman Nelson, M.D.

Last May Dr. Nelson received the Distinguished Service Medal, the highest honor of the Minnesota State Medical Association, in Duluth. His contributions to medicine are legion and far too numerous to list.

Also at this meeting in Duluth the President's Award was given to Drs. Reuben Berman, Lyle Hay, John Earl, Philip F. Eckman and Corrin Hodgson.

Dear Editor:

During my recent visit to Australia, I was able to obtain considerable interesting information about new feeding techniques for cattle and sheep. The technique protects unsaturated fatty acids in the rumen so that meat and dairy products derived from these animals are largely composed of polyunsaturated fatty acids. The potential for a better diet for many people is enormous.

I visited with Joseph Czulak, P.O. Box 20, Commonwealth Scientific Industrial Research Organization (CSIRO), Highet, Victoria, Australia. Mr. Czulak is the coordinator in charge of the Dairy Research Laboratory Program of the CSIRO on the development of dairy products prepared from cattle fed treated feed in order to transform these products from the typical saturated fatty acid state to one rich in polyunsaturated fatty acids. The foods, milk, butter, cheeses, yogurt, and so forth. prepared from the milk produced by these specially fed cattle, appears to be of very high quality, of flavor superior to that of the usually obtained dairy products, but to have somewhat shorter shelf life due to the greater tendency of unsaturated fatty acids to become rancid. Cattle fed this special feed tend to produce a larger amount of milk, helping to offset the somewhat higher cost of the feed. The special feed has been used to produce beef and lamb rich in polyunsaturated fatty acids. According to Mr. Czulak, these meats have a superior taste and palatability. Use of the dairy products and meat rich in polyunsaturates apparently reduces the serum cholesterol and the serum lipids by 10-20%.

The study done so far has been on beef and mutton, rich in polyunsaturated fatty acids produced by allowing animals to grow on ordinary pasture with a final "topping off" of several weeks with the special rations. These rations are groundup sunflower seeds, coated with casine, treated with formalin, which prevent oxidization in the rumen. This technique permits unmodified unsaturated fatty acids to pass into the gut to be absorbed and incorporated into the tissue fat. With about three to six weeks of such feeding, about 28% of the fat of the animal is polyunsaturated. It is not known at this time whether this is an addition of unsaturated fatty acids to a residual amount of saturated fat or whether this is actually substitution of unsaturated fatty acids for the saturated fat. Whatever the mechanism, the result when these meats are fed to volunteers is a significant lowering of serum cholesterol and serum triglycerides.

The average person cannot detect the difference between beef or mutton prepared in the usual way and those prepared with this new process. An occasional person will dislike meat prepared in this way very much but the majority prefer the taste of the mutton. Specially trained taste panels can distinguish quite accurately the meat prepared in this way and even the degree of unsaturatedness obtained. However, these panels cannot distinguish between the polyunsaturated and normal meats when they are prepared with the usual condiments.

I visited with Dr. P. J. Nestal, Department of Clinical Science, John Curten School of Medicine, Canberra, Australia concerning the effect of feeding polyunsaturated food products to patients. Dr. Nestal and his co-workers have found that maximum levels of reduction of cholesterol by restricted diets produce about twice as much of effect as due to diets using polyunsaturated food products prepared by the CSIRO techniques. They have found high levels of cholesterol present in infants within a few days after beginning to feed on cow's milk formulas and on breast milk. The significance of this is not known but it is speculated that studies feeding milk from polyunsaturated fed cows or from others who are ingesting polyunsaturated fatty acids might make a difference in the fatty acid and cholesterol content of the blood of infants.

A paper published in the New England Journal of Medicine was a preliminary report and more detailed investigations are underway which may be reported within the next year. Two recent additional papers are significant—one by Nestal and Bartert—"Metabolism of Palmitse and Linoleic Acids in Man" Differences in Turnover and Conversion to Glycerides,* and one by Whytehm and Nestal, P. J., et al., "Dietary Fat and Coronary Heart Disease: A Review."†

Warren J. Warwick, M.D.
University of Minnesota

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*Clin Sci 40:345, 1971.
†Medical J Aust, I:1155, 1971.

Harold W. Brunn, L.L.B.

Harold W. Brunn, Executive Secretary of the Minnesota State Medical Association, has been elected President of the American Association of Medical Society Executives (AAMSE). He previously served as Secretary-Treasurer and Director. AAMSE is a national organization of executive directors of national, state and county medical associations and societies.

He was elected at the annual meeting of AAMSE Saturday, June 22, held in conjunction with the 123rd Annual Convention of the American Medical Association in Chicago.

Harold Brunn (left) being congratulated by Barnard Hall, M.D. (right), President of the Minnesota State Medical Association.

Valediction*

JOHN J. REGAN, M.D.—Past President

THE LARGELY ceremonial duties of your Association President often obscure other ways in which he can and does serve the State Medical Society. Organizations of physicians, for a variety of reasons, have adopted a structure of complex interrelated forces with an unusual number of checks and balances. Whether the evolutionary development which produced this structure is the result of a subtle paranoia that is endemic in our profession, or is rather the result of trial and error of what makes for effectiveness, the fact is that many medical societies are so ordered. Since that July 23, 1853, when 20 pioneer physicians gathered in St. Paul's first courthouse to organize the Minnesota Medical Society, the predecessor of our Minnesota State Medical Associaton, and elect Dr. Thomas Potts its first president, much organizational development has taken place. The House of Delegates, the Council, the many committees, and the full time staff (which incidentally, prefers not to be called a bureaucracy), all have their function—the President has his. In this rather unusual year, when the President is a relative newcomer to the inner workings of the system, perhaps one of the contributions he can make is a fresh view of the Society, with the added value that beginner's luck brings to such an effort. In our zeal to confront the dangers which assault medicine from without, we stand in risk of failing to be aware of certain dangers which lurk within. I should like to discuss some of the external threats, but for a few moments should like to attend to those internal sources of danger to our society and our profession.

The Minnesota State Medical Association functions adequately for ordinary times—these times are far from ordinary. We limp along attempting new tasks with old methods, only incompletely seeing to the one thing which will assure a reasonable dealing with the problems from without—the health and vigor of our organization, all the while medicine generally is expressing its need for a new populism. The old style consists of old ideas, old words and old faces. From committee to committee, and even from medical society to medical society, one sees a common thread of the same willing and exceedingly competent laborers carrying out the task of organized medicine. Our profession is populated by a band of incredibly talented but often underused individuals who, when assigned a task, perform in admirable fashion—a reservoir of men and women who can contribute much to our society and to the welfare of medicine. The tendency to assign new jobs to old servants must be resisted in our search for broader participation by more physicians. The AMA has expressed an interest in this change by encouraging participation in its affairs by medical students, by interns and by residents. That is all very well—even commendable—but it does not express a populism, only a biphasic distribution, which leaves the physicians in their 30's and 40's under-represented in the halls of medicine and in the important committees of medicine's societies.

Unity is an ideal which few organizations achieve. Union, however, is an achievable objective. Through dignified and courteous debate, we can find the consensus that leads to union and that gives us the ability to face opposition with organized strength rather than with divided weakness. Nowhere is the need for union better in evidence than in our approach to the problem of PSRO during the past year. All across the broad spectrum of organized medicine one sees the failure of physicians to come together on this issue. The AMA has been unable to achieve a common point of view—even in our own MSMA we thought our agreement was to strive for a single statewide PSRO. When the hard negotiations were under way, we did not speak as one—and we got three. As a result, a last ditch effort was necessary to rescue Minnesota from an awkward, unworkable three area designation. Hopefully that is now being modified to two. It could have been one.

The final enemy from within is our own structure. Revision and remodeling of an organization is a rare and seldom thing. Our staff has functioned by tried methods for a long time; the moment of inertia is high; any change will be painful, but one hopes not impossible. New and more violent dangers abound; old organizations solve old problems—old solutions are not adequate today and will be even less adequate to the problems of tomorrow. I would hope the MSMA could consider appointing a blue ribbon committee to study its structure and to suggest change, and even move into effecting that change. I would even hope that outside consultation could be sought—from the AMA, from a management consultant, perhaps even from a medical sociologist.

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*President's Speech before the House of Delegates, May 15, 1974, Duluth, Minnesota.

What of attacks from without? How do we identify the attackers? Who are our friends and, even more important, who are our enemies? Certainly some of the stereotypical concepts of the past may have to be abandoned. Is Senator Bennett, previously our friend, now our enemy? Or is our own intransigence to a new concept the real enemy? Is the businessman with whom we golfed, fraternized and were hail fellow with at the 19th hole, our friend, or is he quite another person across the bargaining table, when he is attempting to establish an HMO for his employees, purportedly to provide them with better medical care, but actually to stabilize and make predictable that portion of his labor costs devoted to health and welfare. Is the politician who once was our friend conceivably another person when he is in quest of power? It has become apparent that old political alliances have lost validity. Recent events will have enormous influence on the balance of power within our system of government. Possibly for the remainder of this century, forces on which medicine has so often been dependent will be in a position of minority. Our task will be to live with new and untried leaders.

Ours is an attractive profession. Ours is a beguiling system, to the degree that many want to be in on our act and do our thing. The planners, the members of what some like to call the "health care team," the nurse who doesn't want to recognize the prescriptive function of the physician, but rather wishes to negotiate something called a "treatment plan." Paraphrasing Winston Churchill, Some plan! Some treatment![1] The social worker who eschews family and community inquiries, who avoids the prescriptive task but who wades unsolicitedly, without direction, without request, or without order, who engages in interminable conferences. Miles of talk and inches of decision. The administrator, who comes into the system to bring order where there was chaos—and there are more people, who comes to make fiscal sense and prices continue to rise, who comes to help and stays to take over. These are antagonists. These are dangers.

Where do we go and what do we do? Do we, like Hamlet, "suffer the slings and arrows of outrageous fortune," or do we "take up arms against them."[2] It is clear that all over the world new forces are taking over. The conservatism of the past is in retreat. Whether we like it or not, we must learn to live with a whole new set of political realities.

Practical experience points to the dwelling place of our friends. The Harris Poll, the Gallup Poll, even the Minnesota Poll, all say that medicine is still an honored profession and that its practitioners walk in the light of public acclaim. To be sure, we have our rascals; every profession does. And so a great and honored medical innovator is indicted and convicted. A leader of the AMA is indicted and convicted. They dishonor themselves, but not our profession. Remember that in the great political upheavals of today there was not a single physician, that of all the learned groups, scandal has touched us least.

Our task is to set aside the tawdry cannards often expressed by the detractors of medicine, more interested in expressing hostility than accuracy, that our profession has lost its relevance to the people and its mission of usefulness. We must give the lie to their misuse of statistics, to their misidentification of problems, and to their exploitation of social, cultural and even racial conflict to attack medicine.

Secondly, we must recognize our friends. The notion that our companions of the golf course always have our interests at heart is nonsense. Often they are the first to exploit our friendship. Indeed, our interests are closer to those of the people we serve. We, like they, are workers. We have no product to sell, no goods to manufacture, no ore to mine. Our concerns are more identical with those of the man in the labor temple than the man of the chamber of commerce. Our skill is our capital, our work is our livelihood.

The real exploiters are those third party interveners who interject themselves into the relationship between physician and patient, who would exploit both, whose interest is not better medical care, but a neater and more profitable balance sheet. What difference if this intervener is an insurance carrier or a federal bureau. He meddles in private and confidential relationships, not to improve care, but to improve profit—to reduce costs, to balance budgets. To deal with these we must have not unity, for that is impossible, but union, derived from broad-based membership in medical societies, examined through energetic discussion, respectful interchange and dignified debate, all of which should lead not to unanimity, but to consensus, and from that to union The labor organizations of America can stand as an example—the Airline Pilots Association—there is and has been an oversupply of trained pilots—there is and has been a zeal to occupy these jobs by many more young men than there are openings—and yet thanks to organization, to common striving, and a unified voice, these men can negotiate with a tough industry and arrive at a contract that pays at maximum $70,000 for a 1000 hour year. How many physicians do you know who earn $70,000 for a two or three or more thousand year? Can we, with our superior training, our superior skills, our superior professionalism, do less? Dr. Roth has said there is nothing a labor union can do for doctors that the AMA can't.[3] True enough, but only if we are truly organized, truly energetic and truly focused on a goal.

Lastly, our historic mission is to bring care to the people. Not to build an empire for a board of trustees, not to satisfy the need for prestige on the part of a group struggling for professionalism, not to give aid to those who would cajole us in the short term and exploit us in the long, but simply to bring, compassionate, scientific medical care to people who are ill. If we do this and at the same time turn a unified face to the world, speak out with calm and dignified authority about those things we know best—if we refuse to panic in the face of shrill and cacophanous abuse, if we establish ourselves on the high ground of good practice, we will never be dislodged by either our friends from within or our enemies from without.

In Proverbs there is a line, "Where there is no vision, the people perish."[4] Ours is the vision, ours are the people.

References

1. On December 30, 1941 Winston Churchill in a speech before the Canadian Parliament quoted from Henri Philippe Petain, Chief of State of the Vichy Government: "Within three weeks England will have her neck wrung like a chicken." To which Churchill replied: "Some chicken—some neck," which brought down the house (U.S. style not British).
2. Roth, Russell B.: Address to North Central Medical Conference, October 21, 1973.
3. Shakespeare, Wm. Hamlet, III i 47.
4. Holy Bible, King James Version, Proverbs 29:18.

Continuing Medical Education

University of Minnesota

Pain Syndromes—September 6-7, 1974.

Pain syndromes of the head, trunk and extremities, their etiology and management will be presented.

Physicians in Family Practice, Internal Medicine and General Surgery are the intended audience.

Radiology of the Gastrointestinal Tract—September 9-13, 1974.

Members of the Minnesota Radiological Society are the invited guests for this annual course. The annual Rigler Lecture will be part of this course. Although intended for radiologists, surgeons and interested physicians are invited.

The Management of Cerebral Palsy—September 9-14, 1974.

Physicians who are responsible for the diagnosis and management of the habilitation of persons with Cerebral Palsy will find this intensive but practically-oriented course of interest.

Hypertension—September 13, 1974.

This one-day course is an extension and elaboration of the nationally televised program which was broadcast from the University in January. The control of hypertension has become the focus of a national health priority.

Obstetrics and Gynecology, 1974: Selected Current Topics—September 18-20, 1974.

It is intended to provide challenging and new material to both specialists in Ob-Gyn, as well as other physicians whose practices include significant responsibility in this subject field. This annual course includes the important John L. McKelvey Lecture.

Fracture Conference

Fracture of the Humerus and Radial Nerve Palsy

DOUGLAS M. DUNCAN, M.D.*; KENNETH A. JOHNSON, M.D.† and
GEORGE R. MONKMAN, M.D.*

Case 1

Dr. Douglas M. Duncan:

A 23-year-old woman was injured in an automobile accident. When seen in the emergency room one hour later, she had severe deformities of her arm and forearm and a wound on the anterior aspect of the forearm (Figure 1).

Dr. Kenneth A. Johnson:

Dr. Bert, would you comment on these Xrays?

Dr. Jeffrey K. Bert:

There are diaphyseal fractures of both bones of the forearm. In addition, there is a displaced fracture of the diaphysis of the humerus. Can you tell me more about the wound on the forearm, as well as the neurovascular status of the extremity?

Dr. Duncan:

There was a 2 cm long wound located anteriorly over the radial fracture site. It appeared to be a puncture wound from within, and it appeared to be clean. Both the radial and ulnar arterial pulsations were easily palpable. The neurologic examination revealed that the patient could not dorsiflex her wrist, extend her metacarpophalangeal joints, or abduct her thumb. No specific sensory loss could be demonstrated.

Dr. Johnson:

What would be your interpretation of these findings, Dr. Robertson?

Dr. Robert C. Robertson:

Since the patient has a fractured forearm, a motor examination might not be very accurate. However, I believe that she probably had a radial nerve palsy.

Dr. Johnson:

Is it significant that no specific area of sensory loss could be demonstrated?

Dr. Robertson:

No, because the radial nerve does not have a consistent autonomous sensory zone, as do the ulnar and median nerves.

Dr. Johnson:

How would you determine which fracture site has damaged the radial nerve?

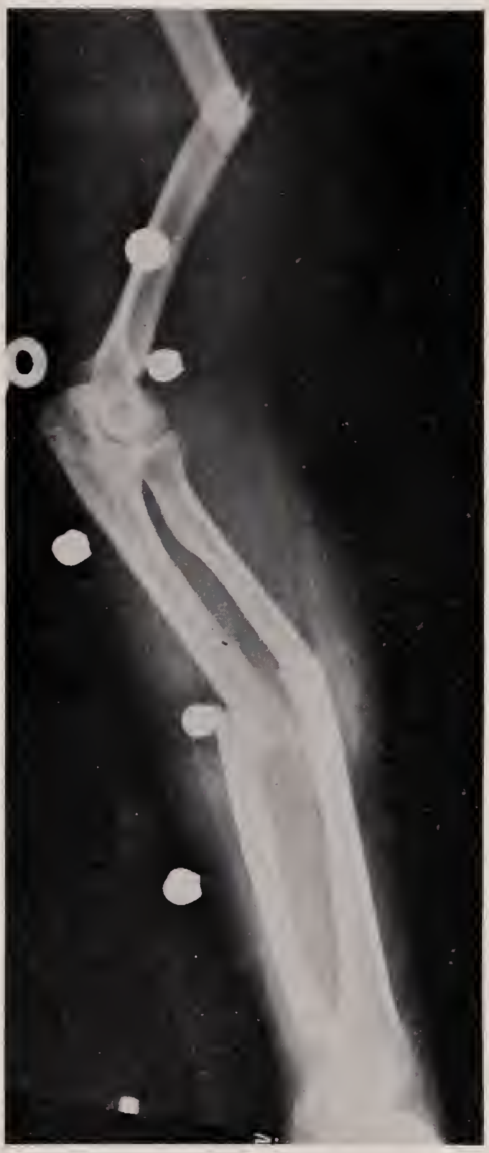

Fig. 1 (Case 1)—Fracture at junction of distal and middle thirds of humerus, and midshaft fractures of both bones of forearm.

Fracture Conference, December 31, 1973.

*Resident in Orthopedics, Mayo Graduate School of Medicine (University of Minnesota), Rochester, Minnesota.

†Consultant, Department of Orthopedics, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Address reprint requests to K. A. Johnson, M.D., Section of Publication, Mayo Clinic, Rochester, Minnesota 55901.

Dr. Robertson:

The extensor carpi radialis longus and the brachioradialis are innervated from above the elbow. If their motor power is absent, then the problem would be a high radial nerve lesion and therefore associated with the humeral fracture.

Dr. Johnson:

It was a high radial nerve lesion associated with the humeral fracture. Dr. Boston, would you discuss your selection of treatment for the forearm fracture with the wound over the midradius?

Dr. Hugh C. Boston, Jr.:

I would debride the wound and close it, and at the same time, I would fixate the fractures with compression plates.

Dr. Joseph M. Janes:

I would prefer to let the wound heal first with a delayed primary closure and then fixate the fractures.

Dr. Franklin H. Sim:

I believe that treatment should depend on the nature of the wound, the duration the wound has been open, and the amount of contamination. In situations like this, I have used either delayed primary wound closure and later fracture fixation or wound debridement and plating of the fractures at the same operation, leaving the wound open for delayed primary closure.

Dr. William H. Bickel:

My experience has been that, if the wound is not grossly contaminated or macerated and if the debridement is thorough, a primary plate or rod fixation with closure of the wounds over a drain is safe.

Dr. Robertson:

Dr. Bickel, if the wound that you have described were located just where you wanted to place a plate, would you hesitate to go through the wound for operative exposure and plate insertion?

Dr. Bickel: No.

Dr. Johnson:

In fact, the forearm wound was treated by initial debridement, followed by delayed primary closure five days later. Ten days after injury, the fractures were fixated with compression plates through separate incisions, neither of which passed through the original wound (Figure 2). If the fracture were treated as described by Dr. Bickel, I am certain he would agree that the patient must be followed extremely carefully in the hospital so that if any symptoms or signs of infection might occur early appropriate treatment measures may be undertaken.

Dr. Belcher, how would you suggest the fractured humerus be treated?

Dr. Darrell C. Belcher:

The humeral fracture is in the region of the spiral groove, and there is a high radial nerve deficit. I think that an exploration of the radial nerve in the fracture region and a plate internal fixation of the fracture would be reasonable.

Dr. Richard S. Bryan:

I would suggest that the radial nerve not be explored and that the fracture be treated by external immobilization. If at six to eight weeks, when the fracture is fairly well healed, there is no electromyographic or clinical evidence of recovery, then the nerve could be explored and sutured if necessary. The delay gives the nerve a chance to recover, and there will be a stable fracture rather than an unstable one if exploration is necessary.

Dr. Sim:

I reviewed the Mayo Clinic cases of humeral fractures with radial nerve palsy. It was a difficult series to evaluate because so many patients were referred and were not treated here initially. One point that impressed me, however, was that most of the patients who were operated on early had radial nerve lesions that could be remedied by the surgical treatment. A second point was that,

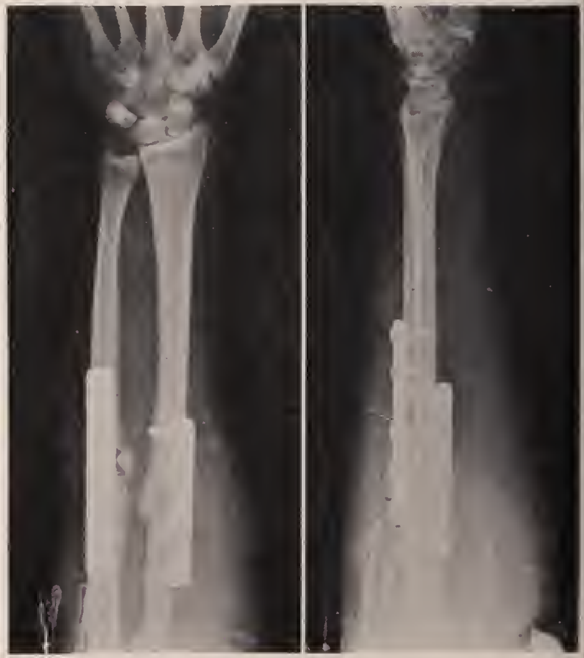

Fig. 2 (Case 1)—Fixation of forearm fractures with compression plates.

when radial nerve lesions were treated expectantly, about 80% of the patients underwent surgery at a later date. Thus, I favor exploration of the nerve within the first several days when there is not so much scar and callus at the fracture site.

Dr. Johnson:

The humeral fracture was treated for 10 days in a bulky compressive dressing, until the forearm fracture was plated. At that time, an olecranon pin was placed and the arm was put in elevated balanced suspension. When the forearm wounds were healed at 19 days after injury, a sugar-tong coaption splint was used to immobilize the humerus, with a sling for forearm support. Eight weeks after injury, the humeral fracture was clinically stable and early callous formation was visible (Figure 3). An electromyogram gave equivocal evidence of radial nerve reinnervation, but the physiatrist believed that there were definite clinical signs of recovery. Three months after injury, the patient could actively extend her wrist and abduct her thumb against gravity, and she was recovering radial nerve function rapidly. Therefore, no radial nerve exploration was necessary.

Discussion

Dr. Duncan:

Most physicians agree that fractures of the diaphysis of the humerus not accompanied by radial nerve impairment are best treated by external immobilization. However, there is no unanimous opinion regarding the treatment of closed fractures of the humerus in which the radial nerve has been damaged. Major disagreement concerns whether to explore the nerve immediately or to delay exploration until eight to 10 weeks after injury if the paralysis persists.

There are advantages to immediate exploration as well as to delayed exploration. If the nerve is explored shortly after injury, there is no scar tissue that has to be cut through; nerve ends are more easily identified and approximated; the nerve, if it has become compressed or trapped at the fracture site, can be extricated, possibly preventing further damage, and recovery probability is improved.[1-4] With early exploration, stabilization of the fracture is accomplished, and if bone shortening becomes necessary in order to approximate the nerve ends, resection of an ununited fracture is not as difficult and surgically traumatic as is resection of a fully united fracture.[4]

The advantages of delayed exploration are that the extent of the damaged area of the nerve is more easily identified; the perineurium is hyper-

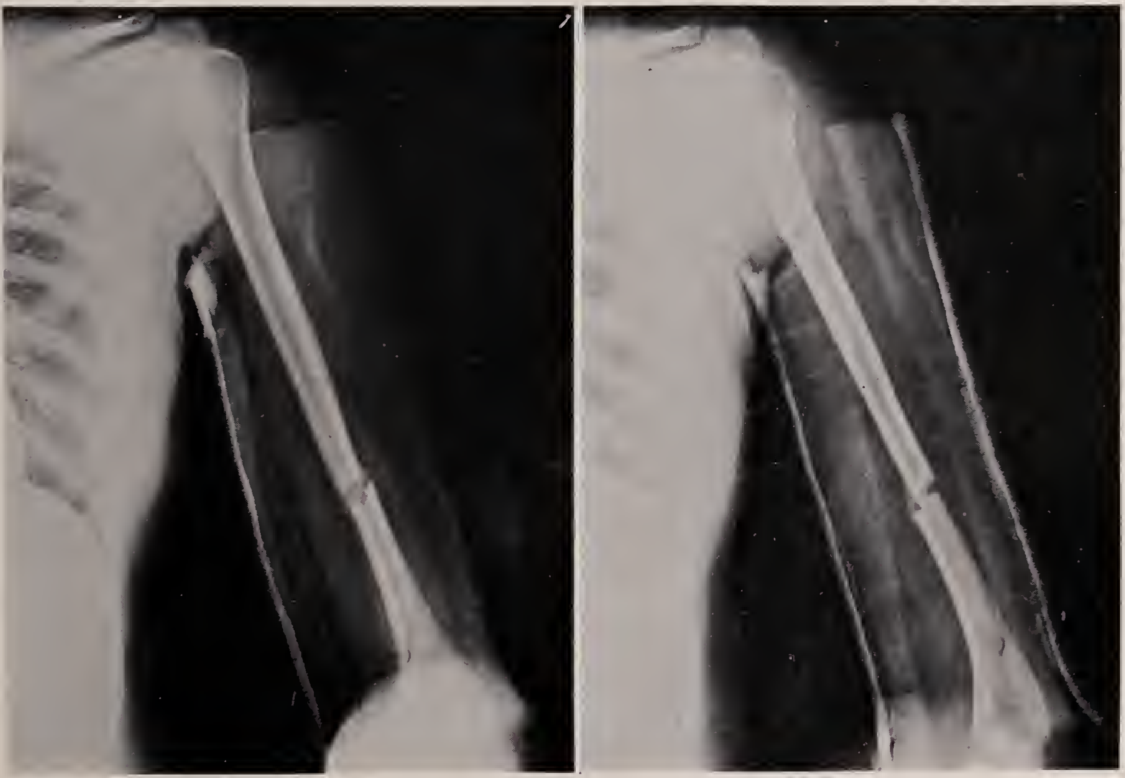

Fig. 3 (Case 1)—Eight weeks after fracture. Humeral fracture was clinically stable and callous formation was visible.

trophied, allowing a stronger and easier anastomosis; and most importantly, unnecessary surgery is avoided in patients in whom spontaneous nerve recovery will occur in the delay period.[1,5] Also with delayed exploration, humeral fractures are clinically united, thereby avoiding the increased incidence of nonunion and infection that is found with the open treatment of humeral fractures.[2,5]

The question remains, "When do you explore the radial nerve early?" If a humeral fracture needs open reduction and fixation, as in displaced segmental fractures, pathologic fractures, or fractures associated with vascular injury, then the radial nerve should be visualized at the time of surgical treatment.[2,5] If a radial nerve palsy occurs or an existing radial nerve palsy is worsened after manipulation, the nerve probably is lying between the fracture fragments and should be surgically mobilized before more damage is done.[3,5] If there is a relatively clean open wound associated with the humeral fracture and radial nerve palsy, the nerve probably should be explored at the time of debridement.[1] Most physicians would agree with these three indications regardless of their views on immediate or delayed exploration.

There are also specific instances when the nerve should not be explored early, such as in a grossly contaminated open macerated wound.[1] Also, if there was an early return of nerve function after initial complete injury or if there was only a paresis rather than paralysis, then the nerve should not be surgically treated early.[2,5] It is the type of humeral fracture with radial nerve paralysis that lies between these rare extremes that continues to provide disagreements concerning early or late radial nerve exploration.

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Robert T. Kelly M.D.

Doctor Robert T. Kelly, a Grand Rapids family physician, was elected to be a member of the Council of Medical Service of the American Medical Association during the closing session of the House of Delegates of that organization's meeting in Chicago June 27. The Council is considered one of the most important committees of the AMA, and is primarily concerned with the financing and delivery of health care.

Doctor Kelly has been a private practice family physician in Grand Rapids, Minnesota, since 1952. He is a past-president of the Minnesota State Medical Association and is a former member of its House of Delegates. He has served as an AMA Delegate since 1968 and he is an active member of the Committee on Medical Service of the Minnesota State Medical Association.

Charles Verheyden, M.D.

Doctor Charles Verheyden, an intern in the Mayo Graduate School, was elected to the Council of Medical Education of the AMA at the same meeting in Chicago. He received his medical education at the University of Texas Medical Branch, Galveston, Texas, from which he graduated in 1973. He is serving his internship at the Mayo Graduate School of Medicine, Rochester, Minnesota. His specialty is surgery.

Public Health

Saint Paul's School-Based Streptococcal Detection Program

HARRY F. KAPHINGST*

During 1971 the Public Health Committee of the Ramsey County Medical Society and the St. Paul Division of Public Health sponsored a school-based streptococcal detection—rheumatic fever prevention program. The program was begun in April 1972 with a grant from the Northlands Regional Medical Program. Although scheduled for continued funding for three years, the second and third years were cancelled as a result of President Nixon's economy moves. Because of the vital role it quickly assumed in the city, plus the grateful acceptance by the general population and medical community, the program was continued even under straightened circumstances.

Medical and scientific procedures followed in the program are based upon recommendations by various departments of the University of Minnesota. Dry swab streptococcal recovery kits are furnished free of charge to school nurses in both parochial and public schools. This service is also extended without charge to all city physicians who wish to participate in the program.

The program is designed to operate as follows. When a teacher notices an "unwell" child, the youngster is referred to the nurse's station. If the nurse determines that the youngster appears to be symptomatic for one of the following: sore throat, tender/swollen cervical glands, tonsillitis, upper respiratory infection, ear infection or earache, fever, rash, joint pains, upset stomach, malaise, or pink eye, she will either refer the child to the family physician, or use one of the provided kits and culture the throat. The used swab is placed directly into the silica jel pouch, securely sealed in the aluminum foil envelope, and either posted in the provided manila envelope, or delivered to the drop box at the Health Center's front entrance. Competent laboratory analysis is completed as soon as possible, and when a "positive" for the Group A Beta hemolytic streptococci is determined, the Division of Public Health immediately telephones the school nurse, or parents, or physician, so that the child may be properly treated. Every effort is made to refer the child to their family physician or clinic for treatment. The program includes 14,000 parochial school children attending thirty-seven schools, which are staffed by thirteen school nurses; and 46,060 public school children attending eighty-three schools, which are staffed by sixty-three nurses.

In addition, and particularly important is the fact that not only is the school population of St. Paul being effectively reached, but several day care centers, neighborhood clinics, and religious family organizations participate in the program.

Of great import is the acceptance of the program by the public. During the reporting out of some 100 "positives," most of the mothers stated how pleased they were with the program. No adverse comment was received. It is now not unusual for the school nurse to receive a call from a mother stating that her child has a sore throat and requests that a throat culture be taken.

Physicians and nurses participating in the program are urged to list the symptoms noted, or reasons for taking the culture, with each specimen taken. More often than not, two and even three symptoms are listed on the accompanying form. A breakdown is delineated for the month of February 1974.

Figure 1 depicts the distribution in the various age categories.

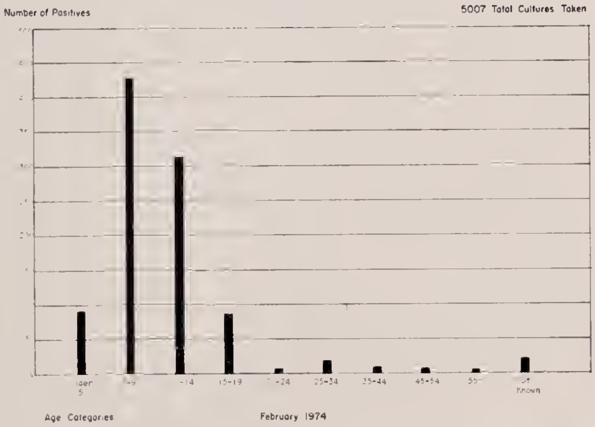

Figure 1

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*Public Health Advisor, U.S. Public Health Service, St. Paul.

Figure 2 describes the frequency of the most commonly stated and observed symptoms.

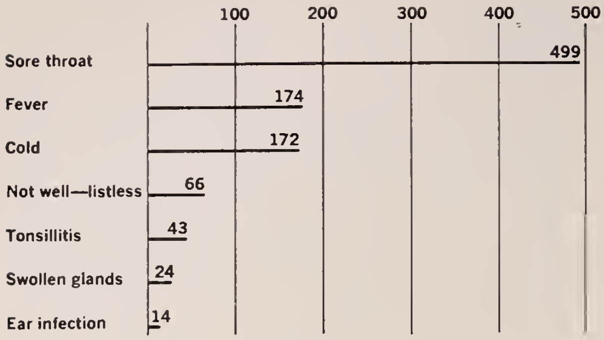


Figure 2

Figure 3 shows the distribution throughout the city. "Out" refers to individuals living beyond the St. Paul city limits.

As can well be expected, "sore throat" was by far the most common complaint, "fever" proved to be a distant second, and "cold" third. Of particular significance is the fact that 202 positive specimens were obtained from "asymptomatic" contacts.

Twenty positive specimens were recovered from the group that for one reason or another were necessary to re-culture. Eighty-four positives were found in the treated population upon completion of the prescribed treatment, and subsequent treatment of these individuals was recommended in all cases.

During May 1974 a screening endeavor was made at one of the city's schools. This consisted of the highest incidence group (five thru nine years), and throat cultures were taken from 200 pupils. This group was a sample of the typical physical condition of the child that attends school on a regular basis. They were all white, from middle- and upper middle-class homes. Each child was observed immediately prior to culturing and questioned regarding the previously stated symptoms.

Comparison Group	
Total number of cultures taken	200
Number of positives found	22
Number of negatives found	178
Total percent positive	11%
Number of positives with symptoms (eight of 22)	36%

Also, nine of the 22 positives had enlarged tonsils, while five were completely asymptomatic.

Asymptomatic contacts of positives who themselves were discovered to be positive	11

As a result of observing and questioning the children immediately prior to their being cultured, the following symptoms were noted in the entire group:

Sore throat	52
Cold	28
Fever	1

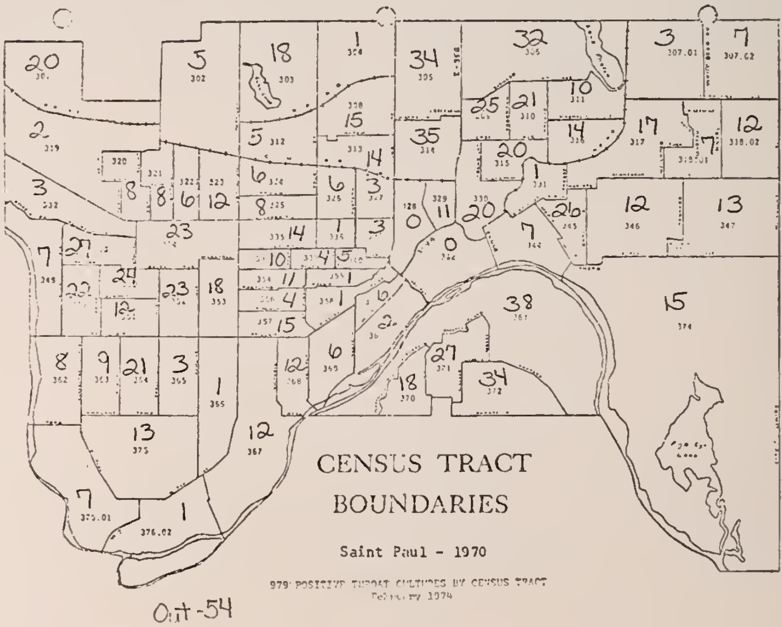
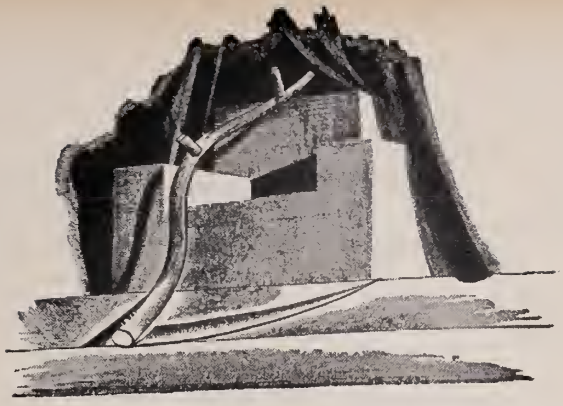


Figure 3



In Memoriam

RAYMOND D. DAVIS, M.D.

Dr. Raymond Davis, retired physician, died June 1. He was 69 years of age, and had practiced for 30 years in Clearbrook and Waseca, Minnesota, and eight years in Stockton, California, on the staff of the Stockton State Hospital.

Dr. Davis was a member of the American Academy of General Practice, the American Medical Association. Waseca County Medical Society and the Minnesota State Medical Association.

His wife survives him.

HAROLD H. FESLER, M.D.

Dr. Harold H. Fesler, 77, St. Paul physician for more than 48 years, died May 30 in Laguna Hills, California, following a long illness.

He was a member of the American Medical Association, the Ramsey County Medical Society and was a Life Member of the Minnesota State Medical Association.

Dr. Fesler is survived by his wife, Ruth, daughter Shirley and a son, Robert.

JOHN L. EMMETT, M.D.

Dr. John Emmett, 70, emeritus Mayo Clinic urologist, died April 18, in Portland, Oregon, where he was associate professor of urology at the University of Oregon. Born in Ogden, Utah, he received his doctor's degree from Northwestern University Medical School.

He was a member of the medical societies of his specialty, and served as president of the North Central Section of the American Urological Association and was a former member of the Board of Editors of the Journal of Urology. In 1964 he was honored by the University of Utah College of Medicine in recognition of his achievements and eminence in his profession.

Dr. Emmett was an Associate Member of the Minnesota State Medical Association and a member of the American Medical Association and the Zumbro Valley Medical Society.

He is survived by his wife, Erma, two daughters, Susan and Sally, and two sons, Dr. John Emmett Jr. of Washington, D.C. and Stephen.

CARL H. COOMBS, M.D.

Dr. C. H. Coombs, Cass Lake physician, died May 14. He was 63 years old. His medical degree was acquired at the University of Minnesota Medical School.

Dr. Coombs was a member of the American Medical Association, the Minnesota State Medical Association and the Upper Mississippi Medical Society.

He is survived by his daughter, Rosalie Wake of Sterling, Virginia.

JUSTUS OHAGE, M.D.

Dr. Justus Ohage, 88, Minneapolis surgeon and former president of the Minnesota State Medical Association, died June 3.

He graduated from the University of Minnesota Medical School and studied two years at the Mayo Clinic in Rochester.

Dr. Ohage was a member of the American Medical Association and the Ramsey County Medical Society. In addition he was a 50 Club and Life Member of the Minnesota State Medical Association.

He is survived by his wife, Esther.

HARRY W. ARNDT, M.D.

Dr. H. W. Arndt, 84, general physician, died January 21, in Apache Junction, Arizona. A graduate of Northwestern University. Dr. Arndt practiced medicine first at Paynesville and later moved to Frazee.

He was a member of the American Medical Association and the Park Region District and County Medical Society and a Life and 50 Club Member of the Minnesota Medical Association.

Dr. Arndt is survived by two sons, Dr. Jerry Arndt of Dallas, Texas. and William of Anoka, and a daughter, Barbara.

DOUGLAS M. GARROW, M.D.

Dr. Douglas M. Garrow, 73, St. Paul physician, died May 14. He had practiced medicine in St. Paul for 40 years.

A graduate of the University of Minnesota Medical School, Dr. Garrow was a member of the American Medical Association and the Ramsey County Medical Society and a Life member of the Minnesota State Medical Association.

Dr. Garrow is survived by his wife, Marian, and daughters, Jean and Betti.

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Book Reviews

THE SOUNDS OF THE NORMAL HEART, by Aldo A. Luisada. M.D.. Warren H. Green, Inc. 1972. Price $14.50.

In this 266 page, amply illustrated book, the author summarizes thirty years' experience with phonocardiography and presents his sixth volume on this subject. The purpose of this work is to contribute to the "training of physicians and to an enrichment of their knowledge." Auscultation was originally based on autopsy findings. The early decades of this century added knowledge of cardiac physiology and techniques of cardiac catheterization that challenged the old concepts. The new basic concept is that "the motion of the heart, transmitted to the chest wall, results in a complex vibratory phenomenon. The heart sounds and murmurs are but a part of this vibration, which is artificially selected by either the human ear or the phonocardiograph." The author describes the auditory system of man as not ideally suited for cardiac auscultation, and shows how these limitations lead to pitfalls in auscultation. He further revises the "classical" areas of auscultation by correlating the actual sound phenomena found within various cardiac chambers and large vessels with sounds recorded over such areas.

Phonocardiography itself, states Luisada, has undergone changes in scope and instrumentation over the last twenty years. It can be defined at present as "the method of recording all vibrations of the precordium." As such it is different from auscultation because: (1) it has a greater scope; (2) it is not bound by the limitations of the auditory system with its selective emphasis of certain bands, its distortion of certain sounds, and its inability to hear other sounds; (3) it may apply itself to a separate study of different vibratory aspects in different frequency bands; (4) it permits accurate timing of the cardiac sounds, and (5) it preserves a permanent document. The work is divided into seven sections: preliminary comments; physics of sound, physiology of sound perception; physiology of heart sounds and murmurs; auscultations; technical aspects of phonocardiography; routine phonocardiographic study; and, the normal vibratory phenomenon of the precordium.

By taking the reader through these seven steps, Luisada attempts to establish that "phonocardiography, if the method is correctly applied through adequate instrumentation and the tracings are correctly interpreted by a trained observer, has a definite superiority over auscultation"—and finally he concludes: "phonocardiography should take its place next to auscultation, which it enriches, guides and checks by means of a fruitful collaboration."

Paul G. Gannon, M.D., Ph.D.
Minneapolis, Minnesota

THE UNCERTAIN MIRACLE: HYPERBARIC OXYGENATION by Vance H. Trimble, Doubleday and Co., Inc., Garden City, N.Y. 1974, 236 pages $6.95.

In the author's words, this book was written as "an attempt to fully explore this little-known field of medicine (hyperbaric oxygenation), to illuminate and ventilate the varied facets of the continuing controversy over its effectiveness and safety, and to indicate its probable future."

A carefully constructed work, aimed primarily at the lay reader, this little volume should be of interest and value to both students and practitioners. Trimble traces the history of HBO from its origins in antiquity through the surprising boom of activity in this country led by Dr. Orval Cunningham for almost two decades following World War I, to the flare of enthusiasm in the early 1960's and the present state of cautious optimism. Although a complete bibliography is lacking, the text is documented with some key references. The role of Hennepin County Hospital and Dr. Claude Hitchcock provides material of special interest to Minnesotans.

John V. Thomas, M.D.
Duluth, Minnesota

WHAT TO DO ABOUT YOUR BRAIN INJURED CHILD by Glenn Doman. Doubleday & Co., Inc. Garden City, New York 1974, 292 pages, $7.95.

When the classic therapies of medicine are incomplete, others move in. This book deals in that area of controversy, the treatment of the severely brain injured child. It sets forth the procedure of a group in Philadelphia who developed the Doman-Delacato method for achieving functional mobility in the brain injured child. In the colorful personal style of Glenn Doman, the physical therapist of the group, a running account of the method is evolved.

However the theory is debatable to pediatric neurologists who in general have been unable to corroborate results of this group. The last documentation in medical circles is a publication in JAMA in 1960 by the group. Otherwise results are presented in the form of generalizations; "results will vary from total success to total failure."

The book is a glowing appeal and tribute to parents and may generate false hope. Pediatric neurologists note that the virtue of the method may be in maximal stimulation of the child's potential, rather than an outcome of the theory presented. The psychiatrist will say that for those parents who are already exerting a maximal effort there will be no escape from guilt.

Dorothy M. Bernstein, M.D.
Minneapolis, Minnesota

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(Continued on page 597)

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Predominant psychoneurotic anxiety

Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequer and/or severity of grand mal seizures m require increased dosage of standard ar convulsant medication; abrupt withdraw may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ir gestion of alcohol and other CNS depres sants. Withdrawal symptoms (similar to those with barbiturates and alcohol) ha occurred following abrupt discontinuan (convulsions, tremor, abdominal and m cle cramps, vomiting and sweating). Ke addiction-prone individuals under caref

respond to one

According to her major
ptoms, she is a psychoneu-
c patient with severe
iety. But according to the
cription she gives of her
ings, part of the problem
sound like depression.
s is because her problem,
ough primarily one of ex-
ive anxiety, is often accom-
ied by depressive symptom-
ogy. Valium (diazepam)
provide relief for both—as
excessive anxiety is re-
d, the depressive symp-
s associated with it are also
n relieved.
There are other advan-
s in using Valium for the
agement of psychoneu-
anxiety with secondary
essive symptoms: the
hotherapeutic effect of
um is pronounced and
d. This means that im-
ement is usually apparent
e patient within a few
rather than in a week or

two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

For further information on this subject, the following references are provided:

1. Henry BW, *et al: Dis Nerv Syst 30*:675-679, Oct 1969.
2. Hollister LE, *et al: Arch Gen Psychiatry 24*:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics 11*:438-441, Sept-Oct 1970.

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(diazepam)
2-mg, 5-mg, 10-mg tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

illance because of their predisposi-
o habituation and dependence. In
nancy, lactation or women of child-
ng age, weigh potential benefit
st possible hazard.
utions: If combined with other psy-
opics or anticonvulsants, consider
ully pharmacology of agents em-
d; drugs such as phenothiazines,
tics, barbiturates, MAO inhibitors
ther antidepressants may potentiate
tion. Usual precautions indicated in
nts severely depressed, or with latent
ssion, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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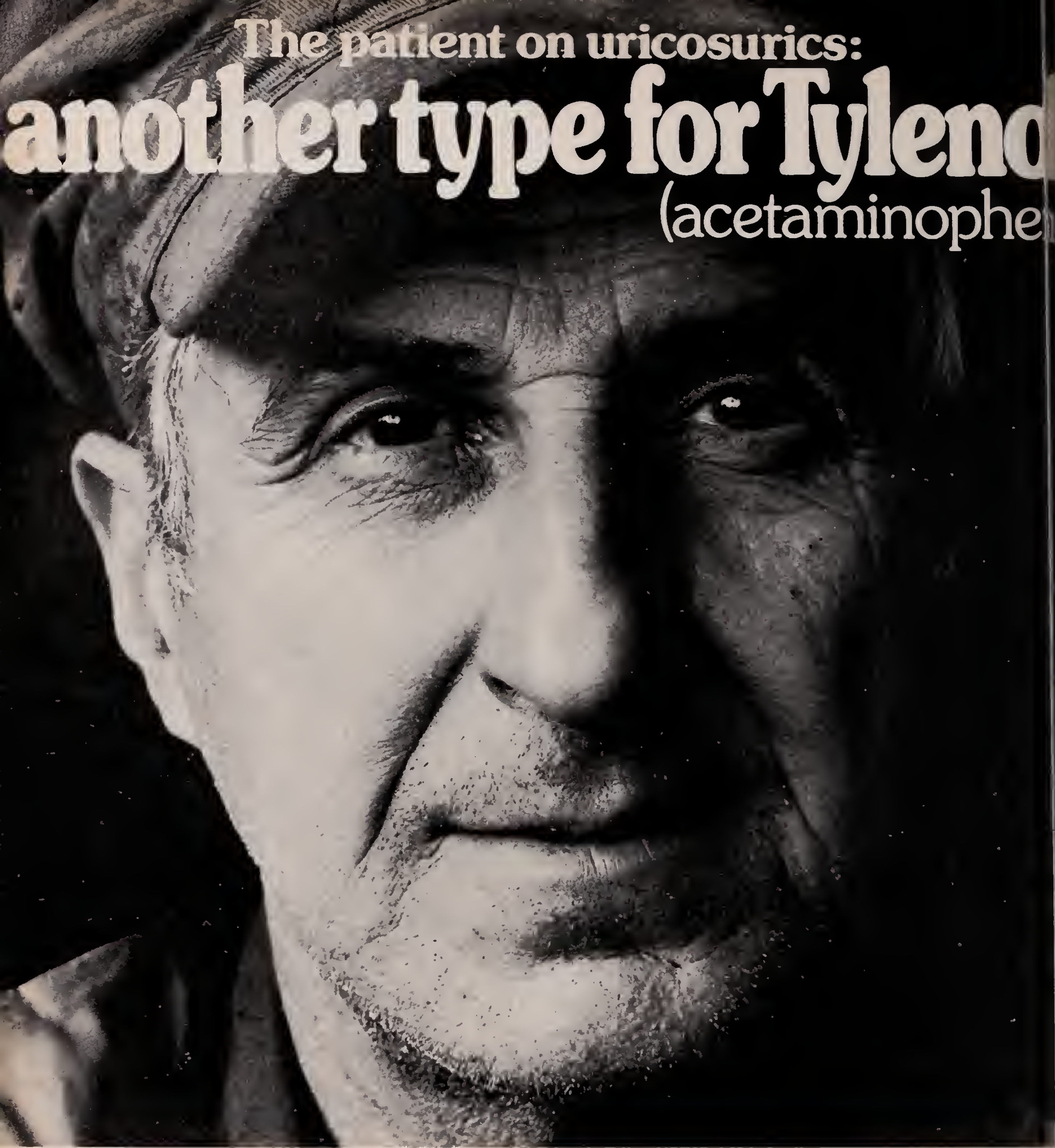

When the patient on uricosuric therapy requires an analgesic, a new problem arises. Aspirin in the usual analgesic doses inhibits the action of uricosurics.[1,2]

TYLENOL (acetaminophen), on the other hand, causes no appreciable uricosuric antagonism[2] and for this reason is preferred over aspirin in the gout patient.

This is only one of several 'types for TYLENOL'—that is, patients who should avoid aspirin. Considering all of them, wouldn't it provide added safety (as well as added convenience) to recommend TYLENOL (acetaminophen) routinely for simple analgesia?

References: **1.** Martin, E.W., et al., ed.: Hazards of Medication. Philadelphia, J.B. Lippincott Co., 1971, p. 511. **2.** Seegmiller, J.E.: Med. Clin. North Amer. *45*:1259-1272 (Sept.) 1961.

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President's Letter

Physicians in Training

In recent years Physicians In Training have demanded a role in the policy decision affecting medicine. They have proposed a variety of changes in working conditions and the quality of residency training. In 1968, through the Residency Committee of the Minnesota State Medical Association, this request for an increasing role was recognized, and efforts were made to actively recruit their membership and involve them in association activities.

Dr. David Crowder, surgical resident at the Mayo Clinic, member of the Executive Committee of the Zumbro Valley Medical Society, delegate to the Minnesota State Medical Association, and a member of the Resident-Intern section of the AMA, is an outstanding representative of the new physicians. I have asked Dr. Crowder to comment on the effects of this admittedly far from complete union of students, interns, residents and practicing physicians.

"About two years ago interns and residents in Rochester seriously questioned their level of participation in organized medicine at the state and local level. After lengthy discussions and some mutual suspicions both the practicing physicians and house officers in our community sat down to create a unique cooperation not known elsewhere in the United States. The result has been a blending of the ideas of the physician-in-training and the established practitioner into goals acceptable to all.

"At this time, Minnesota stands head and shoulders above all other states in providing effective house officer input. Because of its progressive spirit and genuine interest in the views of house officers, the Zumbro Valley Medical Society and Minnesota State Medical Association have earned the deep respect of house officers in Rochester. There are few states where house officers can serve on county medical society committees, show more than token legislative representation, have input to the councils, or for that matter even be eligible to vote for officers. Although we have not always agreed with our more senior colleagues on every issue, the bond of respect and friendship has been established in a way only attainable through direct and honest communications.

"It has been a special privilege for me to work with the Minnesota delegation to the American Medical Association. I have found this group of men to be extremely farsighted with more interest in the future practice of medicine than in short range political goals. They have been true friends to house officers. They conduct their offices with dignity and are a true credit to Minnesota.

"If other states would adopt the progressive attitudes of Minnesota, house officers would not be inclined to look for new groups to represent them. A step which may be necessary although serving to further fragment the physician's voice at a time when government intervention in medicine looms menacingly near. But because Minnesota is willing to listen to all its physicians I can say that in Rochester we wish to continue to work through and not around the Minnesota State Medical Association and its component medical societies.

David Crowder

David F. Crowder, M.D.
Mayo Clinic"

Continuing Medical Education

September

University of Minnesota

Registration information: Office of Continuing Medical Education, University of Minnesota, Box 293, the Medical School, Minneapolis 55455, or by phone (612) 373-8089.

Courses offered in September are:

Pain Syndromes—September 6-7, 1974

Pain syndromes of the head, trunk and extremities, their etiology and management will be presented. Physicians in Family Practice, Internal Medicine and General Surgery are the intended audience, although all physicians are invited.

Radiology of the Gastrointestinal Tract—September 9-13, 1974

Members of the Minnesota Radiological Society are the invited guests for this annual course. Although intended for radiologists, surgeons and other interested physicians are invited to register.

The Management of Cerebral Palsy—September 9-14, 1974

Physicians responsible for the diagnosis and management of the habilitation of persons with Cerebral Palsy will find this of interest.

Hypertension—September 13, 1974

This one-day course is an extension and elaboration of the nationally televised program which was broadcast from the University in January.

Obstetrics and Gynecology, 1974:
Selected Current Topics—September 18-20

This annual course includes the important John L. McKelvey Lecture.

Wisconsin Internal Medicine Specialists

Specialists in internal medicine and related medical fields will hold a two-day scientific meeting on September 13-14, 1974, at the Telemark Lodge in Cable, WI.

The Wisconsin Regional Meeting of the American College of Physicians (ACP) is designed to bring physicians up-to-date on late developments in the field of internal medicine. INFO: George E. Magnin, M.D., 630 South Central Avenue, Marshfield, WI 54449.

Twin City Urological Society

September thru April, excepting December, Pyelogram Conference, 6:00 p.m., Town & Country Club, St. Paul. Contact: Dr. A.S. Cass, St. Paul Ramsey Hospital, St. Paul.

Minnesota Radiological Society

Fall Meeting, September 14 and 15, Cragun's on Pine Beach, Gull Lake, Brainerd. Contact: Marvin E. Goldberg, University of Minnesota Hospitals, Box 292 Mayo, Minneapolis.

Metropolitan Medical Center

Neurology

Conferences, Fridays, 8:30 a.m., Center Building, Conference Room, 900 So. 8th St., Minneapolis. Contact: Mary J. Donner, Metropolitan Medical Center—338-7744.

Audio-Visual Network for Continuing Education

9:00 a.m. in Doctor's Lounge, second Tuesday of each month. 900 South 8th Street, Minneapolis. Contact: Margie Knutson, Metropolitan Medical Center, 338-7744.

Tumor Conference—Cancer

Every Monday except if a holiday. 12:00 noon, 900 South 8th Street, Lower Level Conference Room. Contact: Dr. Lyle J. Hay, MMC, 338-7744.

Mayo Clinic, Rochester

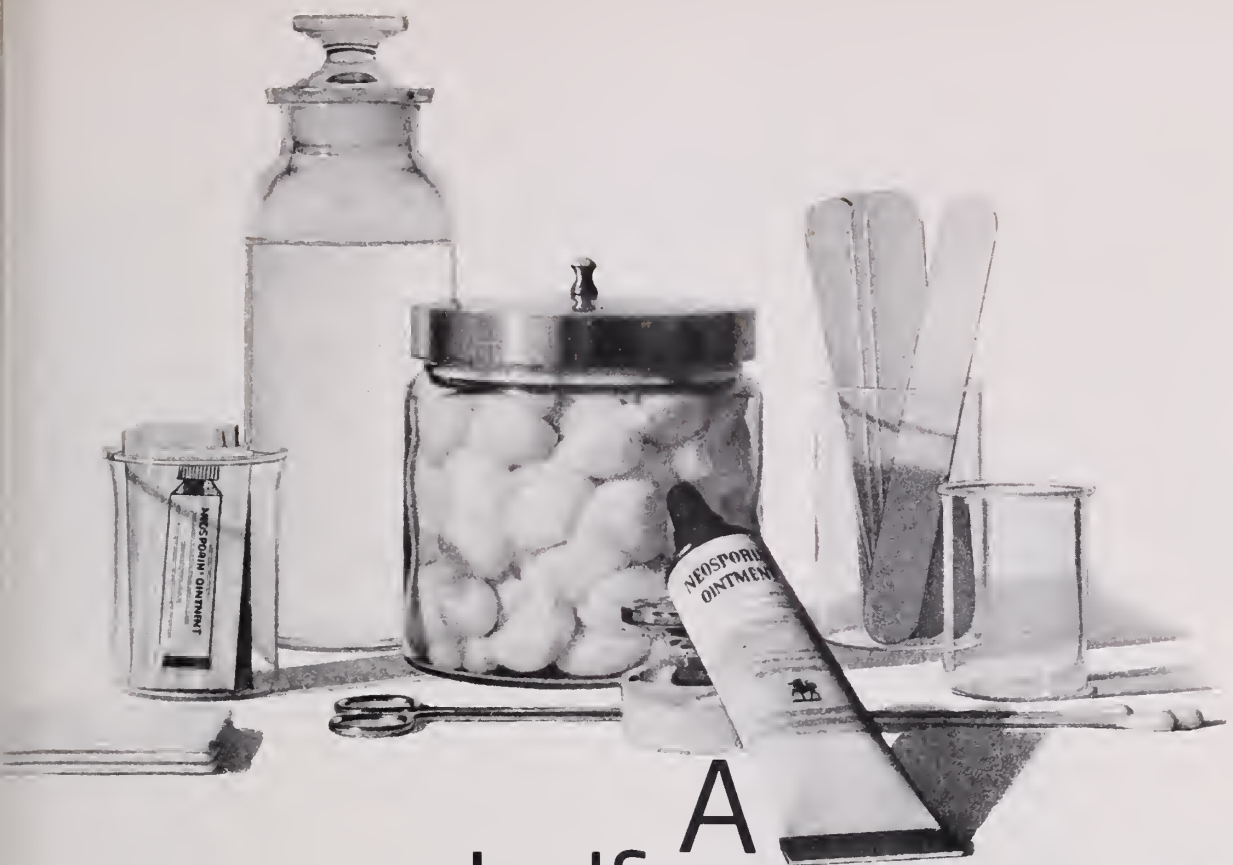
5th International Congress of Electromyography

September 21-24, Mayo Clinic. Contact: Dr. E. H. Lambert, Mayo Clinic.

Health Professionals Drug Abuse Education Project

Drug Abuse

Social Prescription and Illicit Drug Abuse. September 19-21, 5:00 p.m. Thursday and 5:00 p.m. on Saturday. The Young Life Castaway's Club, Detroit Lakes, Minnesota. Contact: Douglas Morgan, 160 Frontier Hall, University of Minnesota. 373-9813.



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ry pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • second-
nfected dermatoses (eczema, herpes, and seborrheic dermatitis)
atic lesions, inflamed or suppurating as a result of bacterial infection.
hylactically, the ointment may be used to prevent bacterial contamination
, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts
nds accidentally incurred, its use may prevent the development of
n and permit wound healing.

INDICATIONS: Not for use in the eyes or external ear canal if the eardrum
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ve burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

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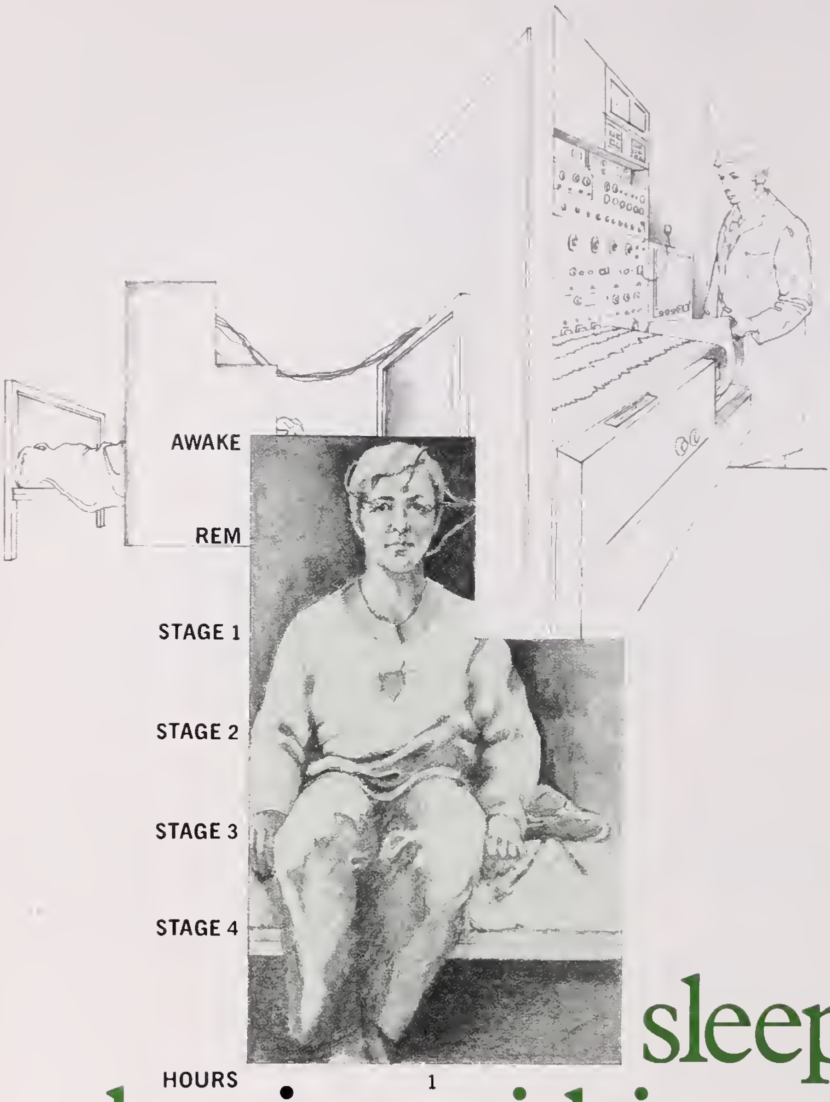

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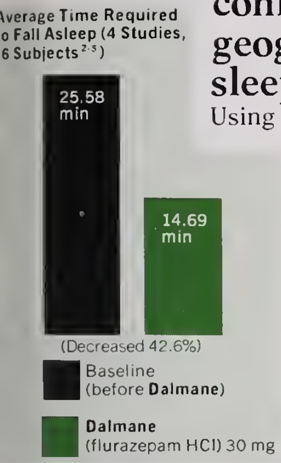

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pressants. Caution against hazardous occupations requiring complete mental alertness
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tential benefits have been weighed against possible hazards. Not recommended for use in
sons under 15 years of age. Though physical and psychological dependence have not been
orted on recommended doses, use caution in administering to
diction-prone individuals or those who might increase dosage.
cautions: In elderly and debilitated, initial dosage should be
ited to 15 mg to preclude oversedation, dizziness and/or ataxia.
ombined with other drugs having hypnotic or CNS-depressant
ects, consider potential additive effects. Employ usual precautions
patients who are severely depressed, or with latent depression or
cidal tendencies. Periodic blood counts and liver and kidney
ction tests are advised during repeated therapy. Observe usual
cautions in presence of impaired renal or hepatic function.
verse Reactions: Dizziness, drowsiness, lightheadedness,
ggering, ataxia and falling have occurred, particularly in elderly
debilitated patients. Severe sedation, lethargy, disorientation and
na, probably indicative of drug intolerance or overdosage, have
n reported. Also reported were headache, heartburn, upset
mach, nausea, vomiting, diarrhea, constipation, GI pain, nervous-
s, talkativeness, apprehension, irritability, weakness, palpitations,
st pains, body and joint pains and GU complaints. There have
o been rare occurrences of sweating, flushes, difficulty in focusing,
rred vision, burning eyes, faintness, hypotension, shortness of
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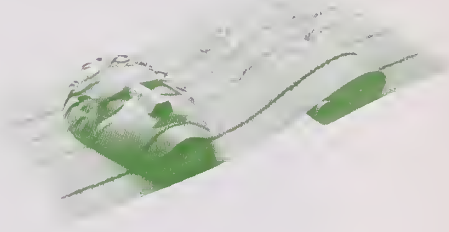

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The Value of Creatine Phosphokinase (CPK) in Determining Intraoperative Myocardial Ischemia

STANLEY EINZIG, M.D.;* WILLIAM G. LINDSAY, M.D.; EDWARD P. TODD, M.D.;
RUSSEL V. LUCAS. JR.. M.D.† ALDO R. CASTANEDA. M.D.
AND DEMETRE M. NICOLOFF, M.D.

Serial CPK levels were drawn in 31 consecutive patients undergoing operations for cardiac defects of which 24 required cardiopulmonary bypass. The mean CPK level was elevated in the immediate postoperative period, reached a maximum on the first postoperative day and reached control levels by the eighth postoperative day. Of potential clinical significance, it was possible to define a rate of decline in serum CPK after the first postoperative day in the patients who had aortic or mitral valve replacement. Further analysis of the data indicated that neither the peak CPK level nor the duration of elevation was influenced by age, ventriculotomy, duration of bypass, bypass itself, or type of chest incision. However, the peak CPK level, (but not its duration of elevation) was related to the duration of aortic cross clamping in aortic valve replacement. We conclude that: (1) an elevation in the CPK level after the eighth postoperative day shall not be related to the operation itself, and supports a diagnosis of myocardial ischemia, and (2) lack of the expected rate of decline in serum CPK after the first postoperative day in aortic or mitral valve patients suggests the presence of myocardial ischemia.

THE CREATINE-PHOSPHOKINASE (CPK) system is the best monitor of acute, ischemic myocardial damage, although elevation of CPK is difficult to interpret. If we knew how long it took the CPK enzyme level to return to normal after an uncomplicated operative repair of the heart, we would be able to distinguish between the inherent insult of surgery and that of an acute myocardial infarction incurred during or shortly after the operation. Undetected postoperative myocardial infarction may cause complications and death. Most parameters of cardiac injury cannot distinguish between the two injuries because the evidence—chest pain, electrocardiographic changes, and metabolic derangement—is the same for both. The feasibility of using an elevation of the CPK enzyme system in patients suspect of acute myocardial damage associated with cardiac surgery is dependent on knowing the normal rise and disappearance characteristics of this enzyme system in otherwise uncomplicated cases of cardiac repair.

This report deals with the temporal elevation and return of serum CPK to normal levels in a group of 31 patients following operative treatment for several different defects. We also examined preoperative or intraoperative factors that might correlate best with the serum CPK level on the first postoperative day. Ideally, by characterizing the behavior of this enzyme in the postoperative cardiac patient, one could continue to use the CPK level as an accurate guide to the presence or absence of ischemic myocardial injury.[9] Other studies have outlined enzyme changes following operation,[2,3,7,15] but we are aware of only two[8,13] that attempted to determine the time required for the CPK enzyme level to return to normal.

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*Fellow Cardiovascular Research Training Grant—#5T01—HE 05222 USPHS.

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See editorial, page 722.

Methods and Materials

CPK levels were drawn preoperatively, immediately postoperatively and thereafter on the first, third, fifth, eighth, and eleventh days in 31 patients who underwent operative repair of a cardiac defect. Twenty-four of these patients (aged three to 72 years) required cardiopulmonary bypass (six aortic valve replacement; four mitral valve replacement; and 14 correction of congenital cardiac disease). The remaining seven patients had thoracotomy for correction of the defect without the use of cardiopulmonary bypass.

Bypass was instituted using a Bentley Bubble Oxygenator which was primed with Normosol R, mannitol, and fresh blood. Hemodilution volume for the oxygenator was 16 cc/kg. Moderate hypothermia was utilized with the lowest esophageal temperatures varying from 30 to 35.5°C. Three of the six who had an aortic valve replacement and one who had tetralogy repair had left coronary artery perfusion. CPK activity was measured by the medical genetics laboratory of the University of Minnesota Hospitals. Using the method described by Tanzer et al.,[12] a sulfhydrate compound was added to the reaction mixture to enhance the activity of the CPK and to give more reproducible results.[10] The measurements were performed with the aid of laboratory kits manufactured by BioChemical Boehringer, Germany.[4] The enzymatic activities were expressed in spectrophotometric units. Normal values for children and adults in our laboratory ranged from 1.0 to 11.0 units/ml. for males, and 1.0 to 6.5 units/ml. for females. Our results were reproducible with a plus or minus 2 standard deviations of 3.2 units/ml. To facilitate comparison the results presented here are expressed as plus or minus (±) the standard error of the mean. Standard statistical methods were used in evaluation of the results.[5]

Results

Duration of CPK Elevation

The serum CPK level was always elevated in the immediate postoperative period, reached a maximum on the first postoperative day and decreased to control levels by the eighth postopera-

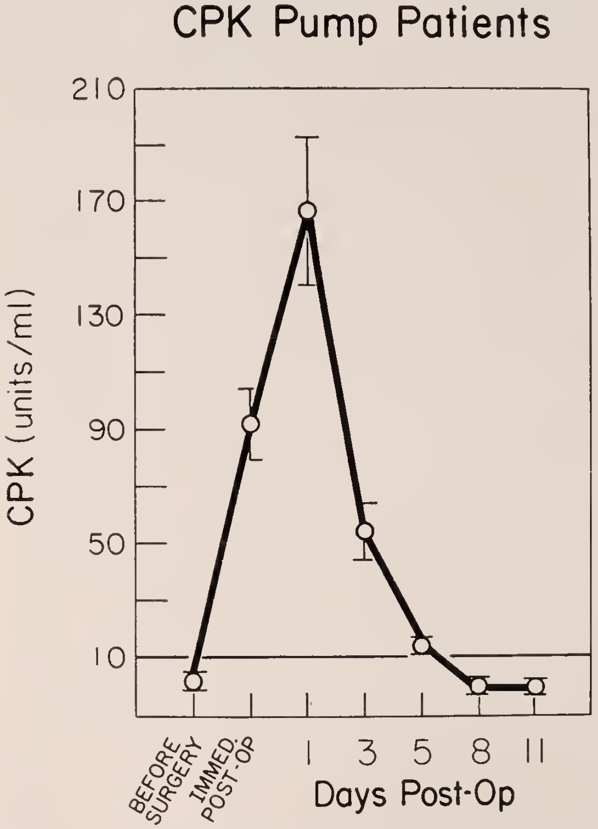

Fig. 1—The mean ± SE (mean) of the serial CPK levels for all pump patients. Peak CPK level was reached on postoperative day one, then fell sharply to reach control levels on postoperative day eight.

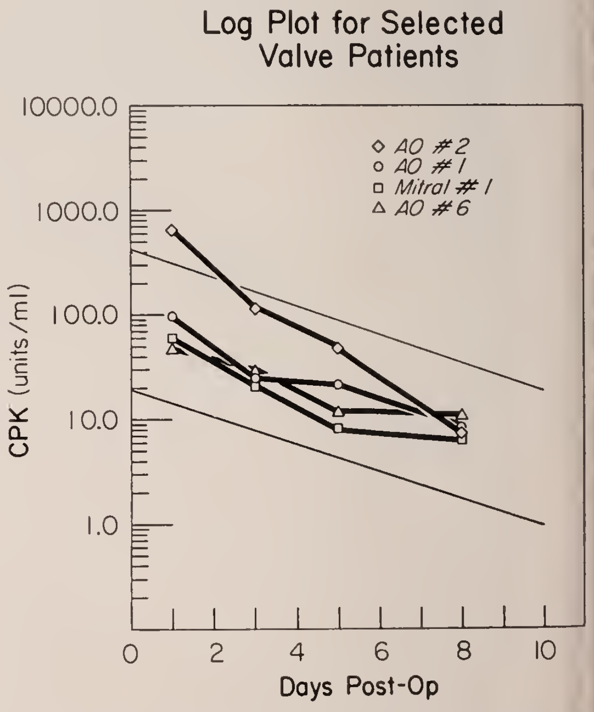

Fig. 2—Serial serum CPK levels plotted semi-logarithmically for selected aortic and mitral valve replacement patients. The patient number corresponds to the number in Table 3. Common slope lines are drawn in. The slopes appear comparable. The common slope for all valve patients was 0.171 ($p < .05$).

tive day (Figure 1). This temporal response was true in all the patients irrespective of age, type of operative procedure, or the level of CPK attained on the first postoperative day.

One patient whose CPK level reached control levels on day three had been on the pump oxygenator during the operative procedure. By the fifth day seven other bypass patients and two of the non-bypass patients had reached control levels. The serum CPK level appeared to drop exponentially from the first to the eighth postoperative day (Figure 1). If one could establish that the rate of decline of serum CPK/time was exponential, as indicated in Figure 1, the serial postoperative CPK levels could be predicted by knowing only the value of the first postoperative day.

Patients undergoing aortic or mitral valve replacement are at highest risk for development of myocardial ischemic episodes during or following surgery. Regression analysis using $\log_{10}$ transformation of the serial CPK resulted in common slopes for the aortic valve and mitral valve patients of -0.161 and -0.192, respectively. The common slope for all the valve patients (aortic and mitral combined) was -0.171 with a standard deviation of ± 0.025. F test analysis for significance revealed that the common slopes derived for the groups separately were internally consistent ($p < 0.05$) and that the common slope of -0.171 derived for the valve replacement patients as a group was significant ($p < 0.05$) and of predictive value (addendum).

The serial CPK levels in several of the valve replacement patients, plotted on semilogarithmic paper, are shown in Figure 2. The parallel lines correspond to the common slope line. Regression

ADDENDUM

To draw a regression line for an individual patient, use the formula:

$$\text{common slope} = b = \frac{Y_8 - Y_1}{d_8 - d_1} = \frac{(\text{difference in } \log_{10} \text{ of CPK})}{(\text{difference in day})}$$

where $b = 0.171$
$Y_8 = \log_{10}$ of CPK on eighth postoperative day
$Y_1 = \log_{10}$ of CPK on first postoperative day (known)
$d_8 = 8$
$d_1 = 1$

$$Y_8 = 7b + Y_1$$
$$Y_8 = Y_1 - 1.197$$

A line between the antilog of Y_8 (predicted CPK on the eighth postoperative day) and the measured CPK on the first postoperative day is drawn on semilogarithmic paper.

To calculate, for an individual patient, the serum CPK level that would be two standard deviations above the expected level on the third or fifth postoperative day, one would modify the formula so that:

$$Y_3 = 2b_1 + Y_1 \text{ and } Y_5 = 4b_1 + Y_1$$

where $Y_3 = \log_{10}$ of CPK on third postoperative day
$Y_5 = \log_{10}$ of CPK on fifth postoperative day
$b_1 = b + 2$ standard deviations of the common slope
$b_1 = -0.171 + 2\,(0.025) = -0.121$

The antilog of Y_3 or Y_5 would represent the serum CPK level two standard deviations above the predicted level. This theoretically should not be exceeded by the measured serum CPK level on the third or fifth postoperative day.

TABLE 1
Non-Bypass
All Thoracotomy Incision Except #3

			CPK Units/ML	
Non-Bypass	Age	Sex	Pre Op	Post Op 1 Day
1—Patent Ductus Arteriosus	18	F	4.4	144
2—Patent Ductus Arteriosus	17	F	3.1	113
3—Valvular Pulmonary Stenosis*	16	M	4.3	189
4—Pericardial Defect†	8	M	5.7	98
5—Mitral Commissurotomy†	33	F	3.0	78
6—Mitral Commissurotomy	21	F	2.6	77
7—Exploratory Thoracotomy	64	M	5.0	80
	Mean ± SE (mean)		4 ± .5	111 ± 16

---

*Midline Sternotomy
†Normal CPK on postoperative day five

analysis for *all* the patients resulted in a common slope of −0.2188. F test analysis for significance, however, showed that this slope could not be applied to every patient ($p > 0.05$). It was not possible to define a significant common slope that could be applied to the pump oxygenator cases as a group. The common slope of the 14 patients with congenital cardiac defects (common slope of −0.2867 ± 0.028) was significantly different than the common slope in the valve replacement patients (0.171 ± 0.025) $p > 0.05$.

Magnitude of the Peak CPK Elevation

The mean maximal postoperative CPK level was the same whether cardiopulmonary bypass was utilized or not (Table 1, Figure 3). A ventriculotomy did not alter the maximal CPK elevation (Table 2, Figure 3). Total pump times ranged from 30 to 167 minutes; duration of total cardiopulmonary bypass did not correlate with the maximum CPK elevation (Figure 4), ($p > 0.05$).

Although the aortic and mitral valve replacement patients were considerably older (ages 37 to 72 years) (Table 3) than the patients undergoing correction of congenital cardiac defects (three to 26 years) (Tables 2, 4), their peak CPK levels were not statistically different (Figure 3). Also, there was no significant difference between the peak CPK levels of patients who had midline sternotomy incisions and patients who had muscle splitting thoracotomy incisions.

When aortic cross clamping time was plotted against peak CPK levels in patients undergoing aortic valve replacement, there was a correlation coefficient of 0.88 ($p < 0.05$) between the duration of the cross clamping and the maximum CPK elevation (Figure 5). The aortic cross clamp

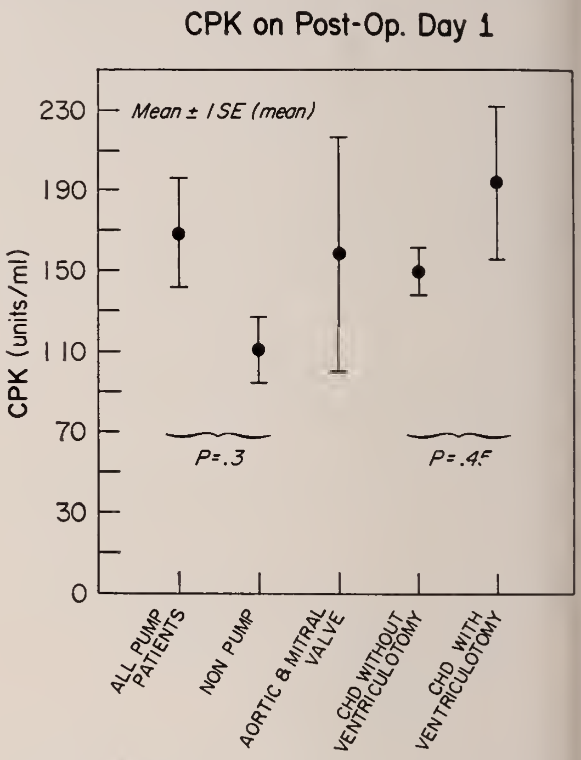

Fig. 3—Mean ± SE (mean) of CPK on postoperative day one. Cardiopulmonary bypass and ventriculotomy did not influence CPK levels on postoperative day one.

TABLE 2
Bypass Cases
All Midline Sternotomy With Right Ventriculotomy Incisions

Pump Cases	Years	Sex	Pump Time (min)	Aortic Cross Clamp Time (min)	CPK Units/ML	
					Pre-Op	Post-Op 1 Day
1—Tetralogy of fallot	18	M	101	36	—	300
2—Tetralogy of fallot	11	F	96	10	10.7	360
3—Tetralogy of fallot‡	4	F	61	12	3.7	166
4—Tetralogy of fallot	5	M	52	7	—	116
5—Tetralogy of fallot	9	M	82	25	8.5	275
6—Tetralogy of fallot*	26	F	136	84	2.1	164
7—Transposition of great vessels (infundibular Invers.)	14	F	55	5	14.4	115
8—Post-op tetralogy of fallot† (pulmonary artery aneurysm)	10	M	74	—	3.3	57
	8	Mean ± SE (mean)			7 ± 2	194 ± 37

---

*Left Coronary Artery Perfusion
†Normal CPK on postoperative day three
‡Normal CPK on postoperative day five

times in patients with tetralogy of fallot did not correlate with peak CPK levels, but the duration of cross clamping was less than in the aortic valve replacement patients. This would tend to indicate that short duration (10-30 min.) crossclamping of the aorta does not cause major detectable myocardial damage.

Discussion

Duration of Serum CPK Elevation

Cohen[6] reviewed the serial changes in serum enzymes after myocardial infarction and found that serum CPK returns to normal levels by the third day. The same time course for CPK release from muscles is seen after strenous exercise in unconditioned individuals.[14] In our patients, how-

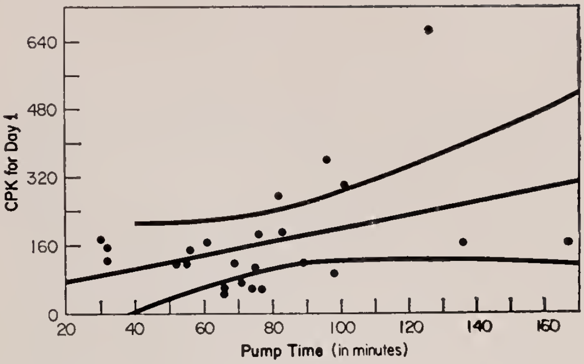

Fig. 4—The CPK on postoperative day one compared to total pump time in minutes. The duration of cardiopulmonary bypass did not influence the maximum CPK elevation ($p > 0.05$).

TABLE 3
Bypass Cases
Valve Replacement
All Midline Sternotomy With Atriotomy Incision

Arotic Valve Replacement	Years	Sex	Pump Time (min)	Aortic Cross Clamp Time (min)	CPK Units/ML	
					Pre-Op	Post-Op 1 Day
1	37*	M	98	76	3.7	94
2	63	F	126	101	6.2	665‡
3	43	M	77	58	2.0	55
4†	72	F	71	50	2.9	72
5†	69*	M	75	66	13.7	108
6	44*	M	66	45	13.8	44.5
						173 ± 99
Mitral Valve Replacement						
1	54	F	66	—	2.8	59
2†	22	M	83	—	—	190
3	46	F	167	—	3.1	164
4	49	F	69	—	2.3	118
	10		Mean ± SE (mean)			113 ± 29
		Total Aortic and Mitral Valve			6.2	157 ± 58

---

*Left Coronary Artery Perfusion

†Normal CPK on postoperative day five

‡Attempt to exclude this patient as an outlier on statistical grounds was unsuccessful (note that this patient had the longest cross-clamp time). There was no statistical difference in peak CPK elevation between aortic and mitral valve patients.

TABLE 4
Bypass Miscellaneous
All Midline Sternotomy With Atriotomy Incisions

Pump Miscellaneous	Age	Sex	Pump Time (min)	Aortic Cross Clamp Time (min)	CPK Units/ML	
					Pre-Op	Post-Op 1 Day
1—Transposition of Great Vessels (Mustard)	3	F	76	—	—	185
2—Transposition of Great Vessels (Mustard)*	3	M	89	—	2.7	118
3—Secundum ASD	8	F	32	—	—	123
4—ASD & PS	7	F	32	—	—	154
5—Valvular Aortic Stenosis* (Valvulotomy)	17	M	30	17	4.8	174
6—Subaortic Stenosis*	8	F	56	45	4.4	149
			Mean ± SE (mean)		4 ± 0.5	150 ± 11

---

*Normal CPK on postoperative day 5

ever, it took eight days for serum CPK values to return to normal, which is consistent with the results of Pyorala,[13] but not those of Dixon.[8] Dixon suggested that a prolonged elevation of the CPK level following thoracic operations could be assumed to represent evidence for myocardial necrosis but had too few patients to perform statistical analysis of his data. One of our patients (Table 2, #8) had a normal CPK by the third postoperative day but only 35 percent of our patients had normal serum CPK levels by the fifth day. We cannot explain why our patients required a longer time to return to normal than those patients reported by Dixon. We can exclude impaired clearance of CPK by the kidneys[1] since renal function impairment was not a problem. We can also exclude the possibility of repeated intramuscular injections,[11] because in our three patients who required repeated intramuscular drug injections there was no correlation between the number of injections and the duration of serum CPK elevation.

Dixon[8] found that patients who had acute myocardial infarctions postoperatively had relatively higher CPK levels on days three to five than patients having an uncomplicated postoperative course.

As the serum CPK of patients who are most at risk for myocardial infarction in the postoperative period (aortic and mitral valve replacement) decline in a predictable fashion, which can be defined by a logarithmic equation (addendum), a deviation from this predicted decline should suggest an additional insult to the myocardium and, thus, aid in our choice of treatment for these patients.

Magnitude of Peak Serum CPK

The second purpose of our study was to determine what preoperative or intraoperative factor or factors correlated best with the level of the serum CPK on the first postoperative day (the maximum CPK level).

Our findings were similar to those of Pyorala.[13] The maximum CPK level was not influenced by: (a) age, (b) cardiopulmonary bypass, (c) presence of a ventriculotomy incision, or (d) duration of cardiopulmonary bypass. Although neither the type of chest incision nor the level of hypothermia could be separated out as isolated variables, neither appeared to influence the maximum CPK elevation. While Pyorala's study did not include any patients who had aortic or mitral valve replacement, we found that these patients were especially interesting to compare. We cross-clamp the aorta during replacement of the aortic valve, thus subjecting the myocardium to significant hypoxia unless the coronary arteries are perfused. On the other hand, mitral valve replacement does not usually interfere with myocardial perfusion, therefore, we were somewhat surprised to find that there was no significant difference between the group peak CPK levels observed in the mitral and in the aortic valve patients, especially since aortic cross-clamping time seemed to be related to peak CPK level in aortic valve patients (Figure 5). The magnitude of CPK elevation in our postoperative patients was dramatically greater than is usually observed in patients with myocardial infarction; although myocardial ischemia may have played a role in elevating CPK, the major factors appeared to be non-myocardial in nature.

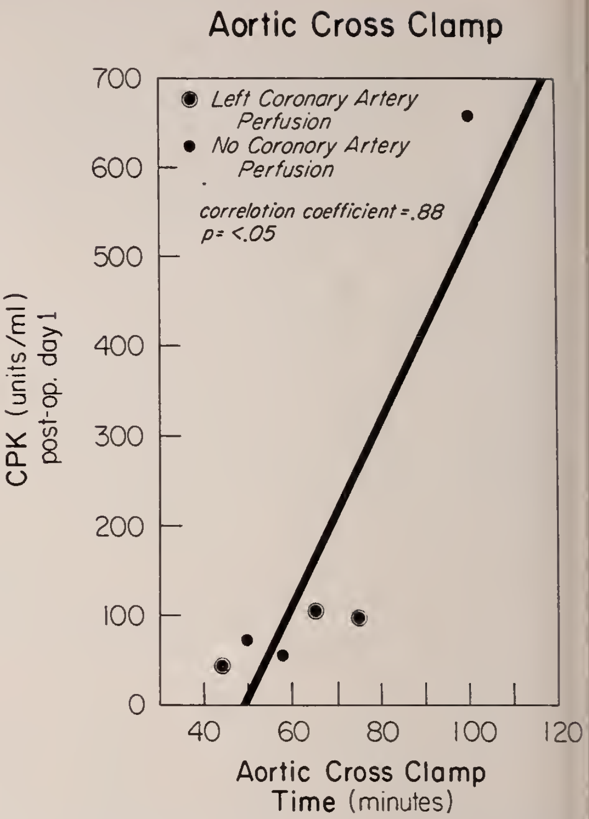

Fig. 5—Aortic cross-clamp time in minutes plotted against the CPK on postoperative day one in patients having aortic valve replacement. There is a significant correlation between the duration of aortic cross-clamping and peak CPK level. The influence of coronary artery perfusion on the peak CPK is difficult to evaluate.

Acknowledgment

The authors gratefully acknowledge the assistance of Dr. Anne Goldman, statistician, Department of Biometry, University of Minnesota, Minneapolis.

References will be found on page 714.

Milroy's Disease, Thrombocytosis, and Strokes

J. T. STURM, M.D.* AND F. W. QUATTLEBAUM, M.D., PH.D.*

The combination of Milroy's Disease, thrombocytosis, and strokes is interesting. It seems logical that the pathologic process common to these three entities is tissue destruction with release of thromboplastic material and activation of the clotting system. With removal of damaged tissue, the activation of the clotting system and its neurologic sequelae ceased. The Thompson procedure has proved to be a satisfactory surgical approach to the treatment of primary lymphedema of the extremities. It should be considered when medical treatment (elevation, ace wraps, and diuretics) fails to produce lasting results. Because of the increasing awareness of intravascular coagulation problems, patients with chronic tissue destruction should be screened for coagulation problems.

ALLEN[1] DEFINED Milroy's Disease as primary lymphedema which is idiopathic, hereditary and congenital. Treatment for this affliction has met with discouraging results. We recently treated a patient with Milroy's Disease whose course had been complicated by a thrombocytosis which was responsible for ten cerebrovascular accidents. The thrombocytosis and occurrence of strokes subsided following surgical correction of the lymphedema.

Case Report

A 27-year-old male with Milroy's Disease was admitted to the hospital in November, 1971, with severe cellulitis over the dorsum of the right foot and anterior aspect of the right leg. The past history is significant in that on ten different occasions he suffered from episodes of left sided hemiparesis and motor speech difficulties, diagnosed by the consulting neurologist as being extracranial right carotid artery occlusion. All of these strokes occurred when the platelet count was above 500,000 per cubic mm, the presumption being that the occlusion was facilitated by the high level of circulating platelets. Angiography had shown a completely occluded right common carotid artery (Figure 2). Each of these ten episodes resolved with bed rest and empirically administered heparin.

The significant physical findings on this admission were limited to the lower extremities and neck: no right carotid pulse was palpable; the legs showed a thick,

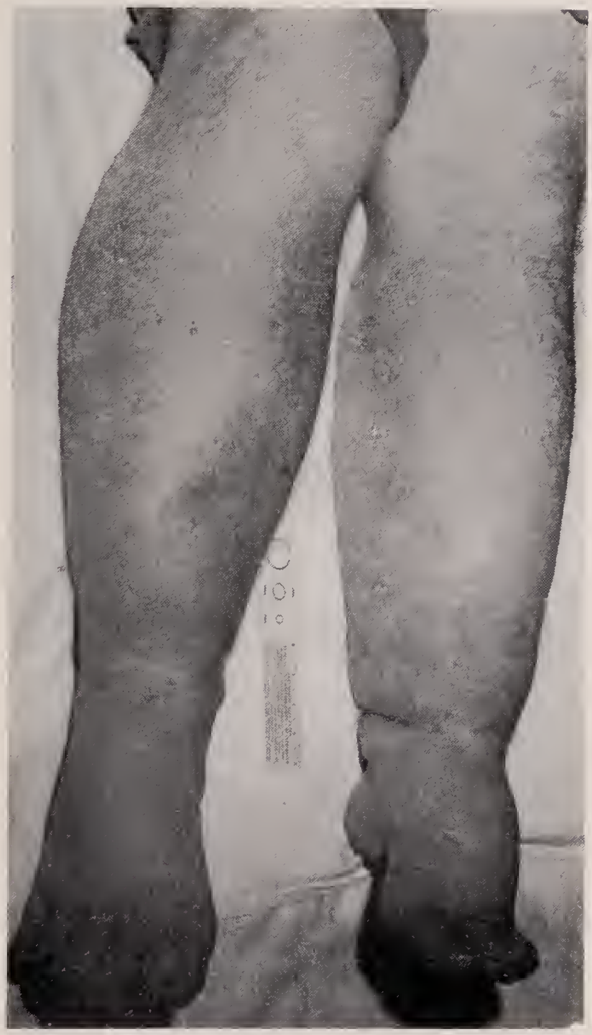

Fig. 1—The legs measured 58 cm. in circumference preoperatively.

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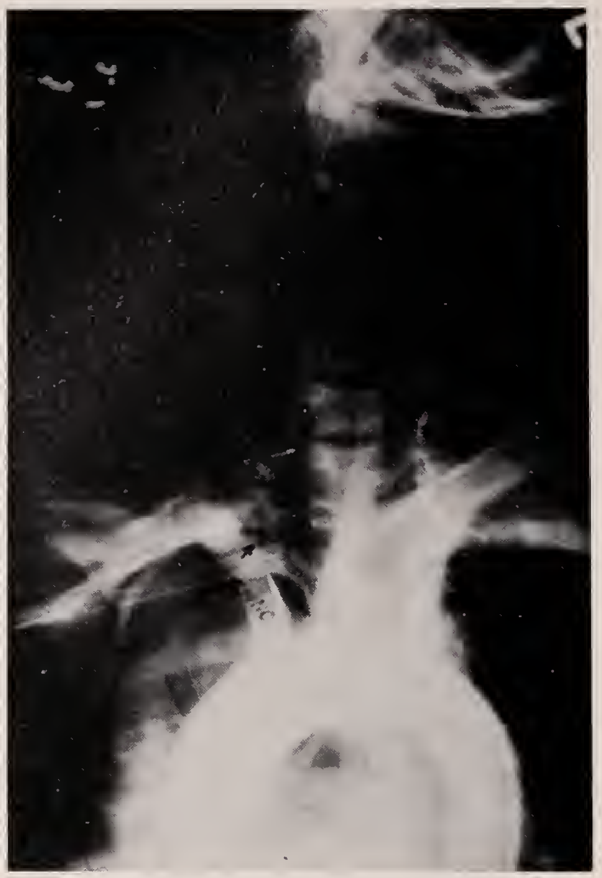

Fig. 2—Arrow shows clotted right common carotid artery. V., vertebral artery; Innom., innominate artery.

brawny, shiny and hairless skin; the right foot and anterior leg were diffusely involved with cellulitis and there was nonpitting edema of both legs from the toes to the knees. Both legs measured 58.0 cm. in circumference at midcalf (Figure 1).

Admission laboratory studies showed a WBC of 22,000 and a platelet count of 600,000 per cubic mm. Hematologic studies and bone marrow aspiration revealed a megakaryocytosis, but otherwise normal findings. Platelet tests showed normal morphology and aggregation. The fibrinogen level was elevated, and fibrinogen split products were present in the serum. Over a two month period, the platelet count rose to 1,016,000 per cubic mm.

Definitive surgical therapy for the lymphedema resulted in a resolution of the thrombocytosis. It was the opinion of the hematological consultant that the patient was releasing increased amounts of thromboplastic material from chronic tissue breakdown in the lymphedematous lower extremities. Release of thromboplastic material can activate the clotting system, producing thrombocytosis, hyperfibrinogenemia, and fibrin split products. Following surgery the platelet count returned to normal (349,000 per cubic mm).

Definitive surgical treatment consisted of staged bilateral Thompson procedures. Severe hyperhydrosis of the feet was a factor in the recurring cellulitis, and for this reason a bilateral lumbar sympathectomy was performed. The patient has been followed for over one year. The legs have decreased in circumference from 58.0 cm. to 43.0 cm. and little edema remains (Figure 3). He is fully ambulatory. Episodically the platelet count increases to 500,000 per cubic mm, but chronic aspirin therapy has prevented further cerebrovascular events.

Discussion

Previous publications[1-4] have shed light on the morphologic and functional aspects of primary lymphedema. Thompson,[5,10] Hugo,[6] and Goldsmith[12] reviewed the surgical aspects of this disease, and have suggested that the most physiologic operation for primary lymphedema is the Thompson procedure.

The fundamental pathophysiologic process in

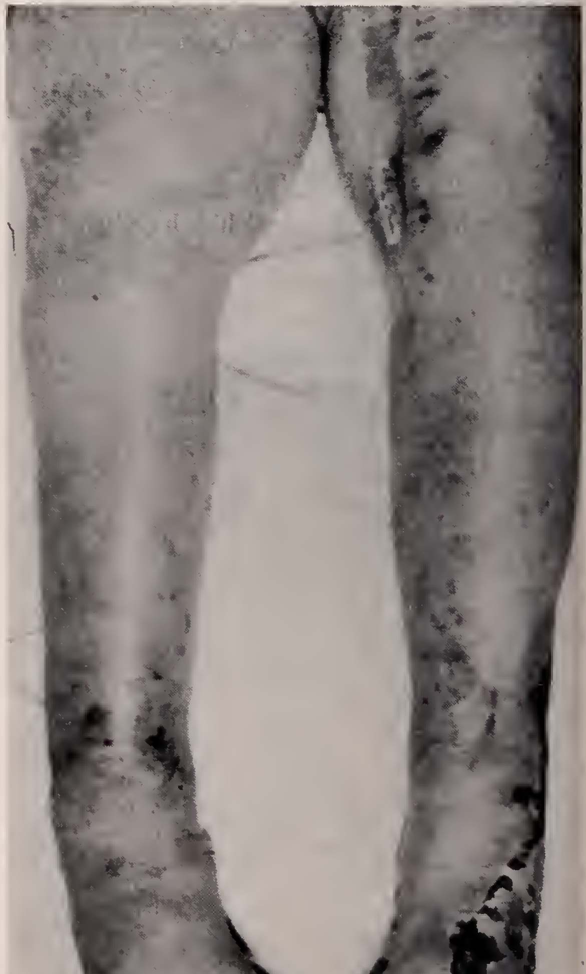

Fig. 3—Postoperatively the legs measured 43 cms. in circumference.

primary lymphedema is the morphologic and functional failure of the subcutaneous lymphatics to drain into the deep lymphatics. The lymphatics in the deep tissues are normal.

The Thompson procedure[5,10] attempts to stimulate anastomoses between the lymphatics in the dermis and the deep lymphatics which run through the muscles and along the major vessels. Preoperatively the legs are elevated, wrapped in elastic bandages, and antibiotics are given if cellulitis is present. The operation involves burying skin flaps, which have been shaved with a dermatome, between the intermuscular compartments medially and laterally.

Thompson[5] demonstrated good or satisfactory results with this procedure in 20 of 22 lower limbs operated upon for primary lymphedema. Comparative preoperative and postoperative radioiodinated human serum albumin uptake studies revealed improved lymphatic flow in each patient. Thompson[10] reported another series of 50 lower limbs with this condition operated upon with his procedure. Results were good or satisfactory in 92% of limbs. He points out that results are not immediate and periods up to one year may be required before observing objective improvement.

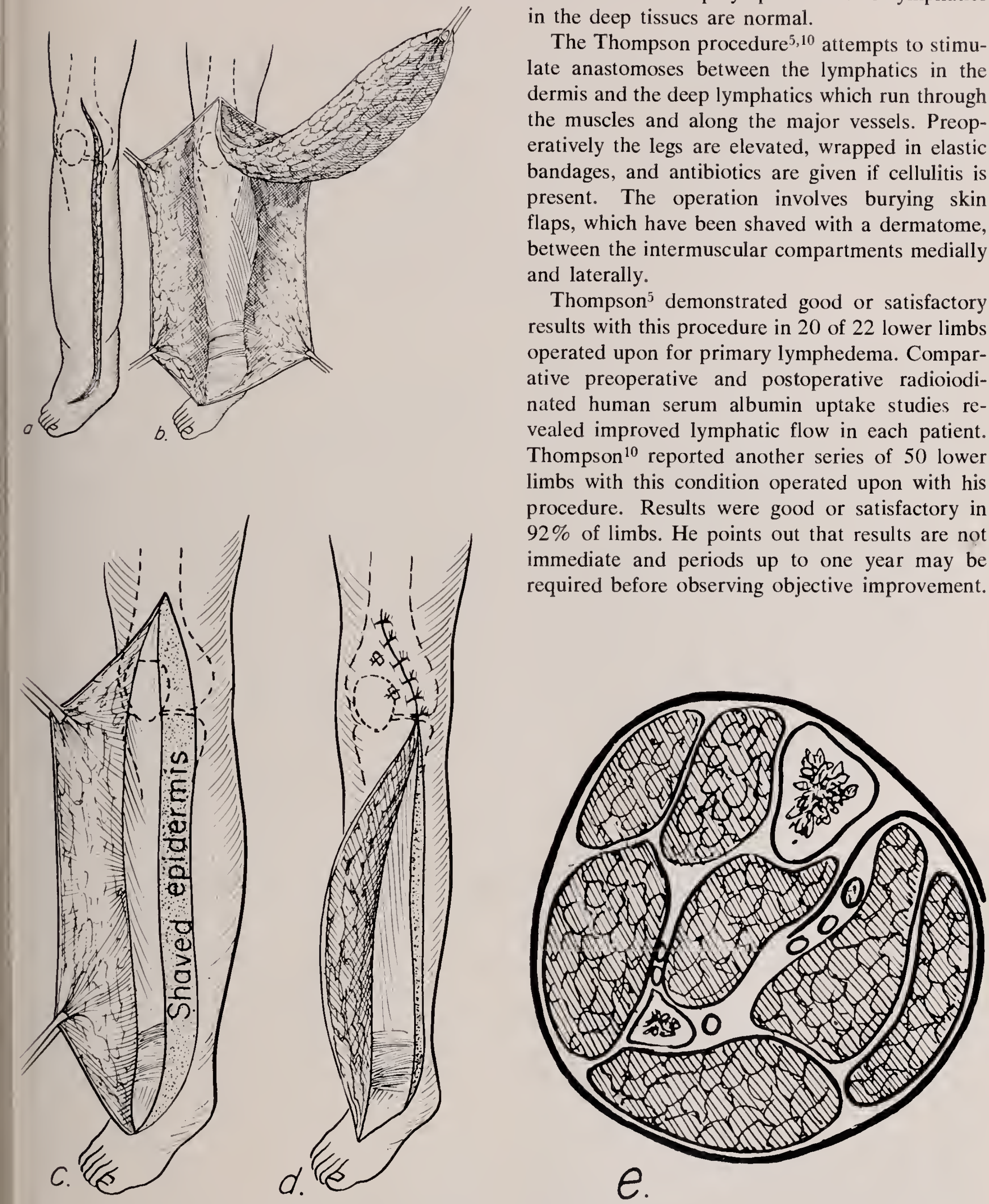

Fig. 4—The Thompson procedure attempts to stimulate anastomoses between dermal lymphatics in muscle. (a) and (b) All subcutaneous tissue including deep fascia is removed. (c) The edge of the incision is shaved with a dermatome. (d) and (e) The shaved flap is buried in the anterior compartment of the leg.

Acknowledgment

The patient reported was studied with the assistance of Dr. Rodger Edson hematologist and Dr. Robert Goldberg, neurologist.

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Morning Session

Screening for Lung Cancer: Prospects and Problems—R. S. Fontana, M.D.		Rochester
Preoperative Recognition and Treatment of Patients with Chronic Obstructive Lung Disease—L. F. Black. M.D.		Rochester
The Approach to the Diagnosis of Hematuria in Children—Edmund C. Burke, M.D.		Rochester
Urologic Aspects of Hyperparathyroidism—R. S. Malek, M.D.		Rochester
The Evaluation and Management of Patients with Unexplained Hypercalcemia—Donald C. Scholz, M.D.		Rochester
Panel: The Management of Prostatic Cancer.	John Lester, M.D., Moderator	Mapleton
Radiation Therapy	Roger Cupps, M.D.	Rochester
Hormonal Therapy	Robert Myers, M.D.	Rochester
Surgical Management	William Furlow, M.D.	Rochester

Afternoon Session

Results of 250 Consecutive Polypectomies through the Flexible Fiberoptic Colonoscope—Santhat Nivatvongs, M.D.		Minneapolis
	Stanley M. Goldberg, M.D.	Minneapolis
Endoscopic Transduodenal Cholangiography and Pancreatography. Indications and Results—John E. King, M.D.		Rochester
Hepatitis in an Elderly Lady with a Positive Mono Test—David Pope, M.D.		Janesville
	D. K. Ohrt, M.D.	Mankato
Mortality of Cholecystectomy in a Small Community Hospital—Mansur Taufic, M.D.		Austin
Vaginal Recurrence after Hysterectomy for Carcinoma-in-Situ of the Cervix—Edgar E. Heller, M.D., D. K. Ohrt, M.D.		Mankato
Dressler's Syndrome Post Myocardial Infarction with Response to Corticosteroids—Marcus A. Keil, M.D.		Albert Lea
What's New ! ! ! ! ! ! Concise Perspectives! ! ! ! ! !		
Computed Tomography—A New Horizon in Neuroradiology—	Hillier L. Baker, M.D.	Rochester
Highly Selective Vagotomy for Peptic Ulcer—Martin A. Adson, M.D.		Rochester
Tomography During Excretory Urography—Joseph Segura, M.D.		Rochester
The Management of Chronic Active Liver Disease—E. Rolland Dickson, M.D.		Rochester

Mail all correspondence to: Executive Secretary: Miss Ethel A. McClane, 1726 North Fourth Street, Mankato, Minnesota 56001.

Symptomatic Metastatic Melanoma of Spleen

CHARLES N. VERHEYDEN, M.D., PH.D.*;
JOHN A. VAN HEERDEN, M.B., CH.B., F.R.C.S.(C)* AND J. AIDAN CARNEY, M.B.*

Splenomegaly due to metastatic malignant melanoma caused pain that was relieved by splenectomy. The rarity of isolated metastases to the spleen and the hypotheses explaining this are discussed.

METASTATIC NEOPLASM to the spleen is not an unusual autopsy finding in cases of disseminated malignancy.[1] In about one-third to one-half of the cases, metastatic deposits of tumor in the spleen are uncovered only after microscopic examination of blocks of tissue that grossly appear normal.[1,2] Only rarely does a spleen that contains metastatic tumor present a surgical problem either because it has become painful[3] or because it has ruptured.[4]

In this report we document the value of splenectomy in symptomatic metastatic malignant melanoma to the spleen and discuss the rarity of metastases to the spleen.

Fig. 1—Scintigrams showing splenic filling defects.

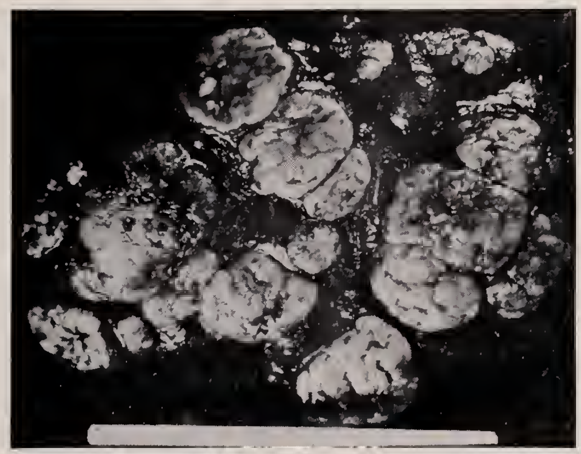

Fig. 2—Cut surface of spleen exhibiting multiple tumor nodules up to 4 cm in diameter.

Case Report

A 37-year-old man noticed a "mole" on his left lower anterior neck for the first time in November 1972. The "mole" grew and changed in color from brown to purplish black. It became superficially ulcerated in December 1972. The patient consulted a physician, who excised the lesion; microscopically, it was a malignant melanoma that had invaded the reticular dermis. In January 1973, when the patient presented at the Mayo Clinic, there was no clinical or laboratory evidence of residual or metastatic tumor. Further surgical treatment consisted of removal of the skin surrounding the site of excision of the melanoma and dissection of the left deep jugular lymph nodes. No residual tumor was found at the site of excision, but a single node high up in the deep jugular chain contained metastatic malignant melanoma. Clinically, the neoplasm was graded stage 1B. Chemotherapy was not advised.

The patient returned on June 15, 1973, complaining of malaise, fatigue, and weight loss (6.5 kg [14 lb]).

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Examination showed a firm, fixed, nontender mass in the left submandibular area. The liver and spleen stretched two and four fingerbreadths below the right and left costal margins, respectively. Pain in the left upper quadrant was associated with deep inspiration. The liver-spleen scintiscan (^{99m}Tc) showed no abnormality of the liver but at least one, and probably two, localized defects of activity in the spleen; the scan was thought to be consistent with metastatic tumor (Figure 1). The neck mass was removed; microscopically, it was metastatic melanoma. The left upper quadrant pain became persistent, and, in addition, pain was felt in the left shoulder to such a degree that splenectomy was advised for relief of pain. Laparotomy (June 29, 1973) disclosed diffuse melanomatous deposits in both lobes of the liver and perisplenitis. The planned splenectomy was performed. The enlarged spleen weighed 900 g. The cut surface of the spleen exhibited multiple whitish tumor nodules (diameter, up to 4 cm) (Figure 2); microscopic examination confirmed anaplastic metastatic malignant melanoma (Figure 3).

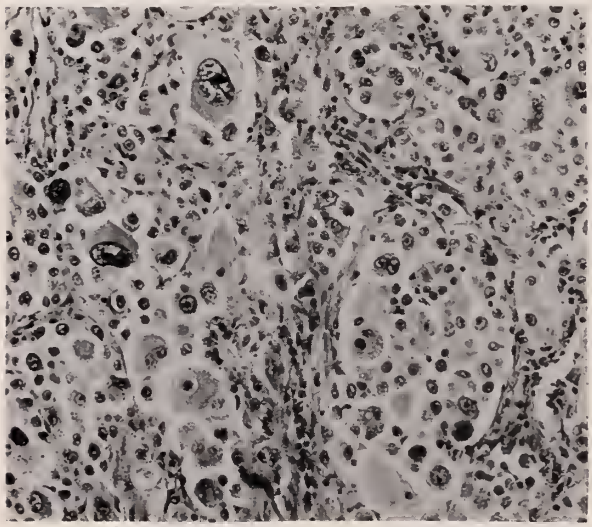

Fig. 3—Micrograph of splenic tumor nodule showing anaplastic tumor cells. No melanin pigment is seen. (Hematoxylin and eosin; x100.)

Discussion

The neoplasms that most commonly metastasize to the spleen originate in the breast, lung, ovary, and skin (melanoma). Among these, malignant melanoma produces metastatic deposits in the spleen most frequently.[1] This appears to be directly related to the metastasizing potential of this neoplasm and partially to its ability to involve a multiplicity of organs when it does metastasize.

The frequency with which splenic metastases are found in patients with metastasizing tumor depends on the stage of the neoplasm at the time of death and the diligence of the pathologist in searching for such lesions. Harman and Dacorso[5] examined the spleens of 30 patients with widespread metastases* and found metastases in 33% of them; in a much larger series, Berge[1] found splenic metastases in only 7.9% of patients with metastasizing carcinomas. Special techniques for examination of the spleen (in which multiple sections are taken for microscopic examination) frequently yield additional unsuspected cases of splenic metastasis. Harman and Dacorso[5] found that the incidence of metastasis thereby increased to 50%. Berge[1] selected 11 random blocks from the spleen in 35 consecutive cases of widespread metastatic malignancy in which there was no gross evidence of splenic metastasis and found that microscopic splenic metastasis was present in 7 (20%) of the cases. Instances in which the spleen is the sole visceral organ to be involved in secondary neoplastic growth are indeed rare. Only 10 such cases have been described; the varied primary sites have included rectum,[6] ovary,[7] nasal mucosa (melanoma),[8] prostate,[9] and lung.[10]

Although not uncommon, metastatic tumor to the spleen is not usually symptomatic and is unrecognized clinically, although occasionally splenomegaly is present.[1] Rarely, symptoms of an acute abdominal emergency secondary to spontaneous rupture of a metastatically involved spleen have been reported.[3,4] Splenic infarction with associated perisplenitis has been attributed to tumor emboli. The pathologic examination in the present case showed that necrosis of splenic metastases, with secondary perisplenitis and involvement of the parietal peritoneum, caused pain.

Because splenic metastases are usually found in patients with widespread malignancy,[1] splenectomy for metastasis, as expected, is not curative and has little effect on the course of the disease. In our case, the fact that an enlarged spleen, containing presumed metastases, was producing significant symptoms despite a normal chest roentgenogram and negative hepatic scan (although the liver was enlarged) justified abdominal exploration. Although the massive metastatic deposits of malignant melanoma in both lobes of the liver indicated that splenectomy could not be expected to alter the course of the disease, the desired effect of surgery—pain relief—was achieved.

The mechanisms of spread of cancer to the spleen were summarized by Willis[11] as follows:

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*Defined as metastases of a tumor to at least one organ in the abdominal as well as the thoracic cavity.

A. Direct nonmetastatic
   1. From contiguous tumors
   2. Via lymphatics
   3. Via splenic veins
B. True embolic metastasis via splenic artery

Arterial embolism is the primary mechanism of splenic metastasis.[5,9,12,13] Nonmetastatic involvement does occur by contiguous growth, but penetration of the capsule is unlikely.[14] Goldberg,[15] in two cases; demonstrated metastasis in the spleen that was propagated by way of lymphatic vessels, but this also is rare. Although retrograde invasion of the spleen through the splenic vein is a possibility, there is no evidence that this actually occurs.

Several hypotheses have been offered with respect to the infrequency of solitary splenic metastases and the more common involvement only in cases of disseminated neoplastic disease:

1. *The mechanical barrier of the capsule.* The efficacy of this has been demonstrated.[14,16]

2. *Lack of afferent lymphatics.* The splenic parenchyma does not have afferent lymphatics. Lymph vessels are confined to the capsule and trabeculae. This theory has been suggested frequently[4,16-19] because virtually all secondary growths occur in the red pulp.[16]

3. *Splenic contraction.* Kettle[20] in 1912 stated that because the spleen was a "contractile organ" it was difficult for malignant emboli to "make good their footing and grow progressively." Some authors have concurred[9,17,18] but others have discounted splenic contraction as a factor;[5,16,19] Harman and Dacorso[5] pointed out that the kidney and pancreas, which are less contractible, have approximately the same incidence of metastatic involvement as the spleen. In addition, the lungs, which are infinitely more contractible, have a much higher incidence.

4. *Angle of origin of the splenic artery.* Krumbhaar[9] referred to this as a possible factor limiting metastasis to the spleen and Milton[16] discounted it; there is no concrete evidence for either viewpoint.

5. *Lesser number of tumors spread by arterial embolization.* Carcinomas of the lung, breast, and ovary, as well as melanomas, are held to be responsible for the majority of splenic metastases (54%);[1,11] several investigators have shown relatively high incidences of splenic metastases in carcinoma of the breast[2,18,21] and lung[2,17] and in melanoma.[21] Since cancers of the breast and lung are not rare, the veracity underlying this hypothesis must be questioned, even though all other metastasizing tumors infrequently involve the spleen.

6. *Filter-like action of lymph nodes, liver, and lungs.* Because arterial embolization is the mechanism by which the spleen is involved in metastatic disease, Harman and Dacorso[5] proposed that the lymph nodes, lungs, and liver act as barriers through which metastatic emboli must pass. When tumor emboli do enter the general circulation, however, only three sites are more frequently involved than the spleen: liver (tumors not drained by portal vein), skeleton, and adrenals.[1] Frequency of involvement of the pancreas[5] and the kidney[18] closely parallels that of the spleen.

7. *Increased oxygen concentration and decreased carbohydrate concentration.* Studying an experimental tumor, Miller and Milton[22] noted that the initial growth of the tumor in the spleen was slower than that in the liver. Miller[23] later demonstrated that the size of these implanted lesions was significantly greater in the liver than in the spleen. This phenomenon has been attributed to an increased oxygen tension and decreased carbohydrate concentration in the spleen as compared to the liver.[11,16,17,23] Milton[16] pointed out that the spleen shares these characteristics with other areas that are also infrequently involved in metastatic disease: muscle, bowel wall, urinary bladder, and prostate.

8. *Antineoplastic activity of the spleen.* This hypothesis has been hotly debated by investigators for many years. Most authors reject the theory that the spleen possesses any immunity to neoplastic disease,[1,17,18,24,25] but others believe that it does.[9,19,26-28] Two mechanisms have been proposed for the action of the spleen on metastatic cells. Phagocytosis was suggested by Krumbhaar,[9] who found nodules in the spleen, some of which he thought were tiny neoplasms surrounded by fibrous tissue. This has been criticized as a possibility because other organs of the reticuloendothelial system manifestly fail to demonstrate this capacity.[17,28] A second possible mechanism of action is the production of a diffusible tumor-resisting substance by the spleen,[19,28] but there is little evidence for this. Nolan and colleagues,[26] however, devised an interesting ex-

periment in which pig spleens with implanted mouse melanoma were perfused. The same tumor was introduced into mice and then cellular elements of the perfusate or of the spleen itself were injected for several days. The injections were protective to the host in a dose-dependent relationship. Metastatic tumor foci appeared in the splenic pulp but were surrounded by lymphocytes and then disappeared, whereas those on the splenic surface did not show lymphocytic invasion and persisted.[26]

Many facets of splenic metastasis are, therefore, vigorously debated issues. A relationship between metastatic involvement of the spleen and heterotopic splenic hemopoiesis has even been proposed[29] and also rejected.[16] Much of the discussion, however, is academic, because the effects of the metastases are rarely of importance.[11] The frequency of infarction in cases of splenic metastasis is greater than that in controls,[1] but cases of infarction, perforation, or rupture present infrequently,[11] although they have been reported.[4]

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*He had not gained a higher rank in the service than that of Lieutenant. The fact is, that Jack was poor, and his brother officers as tough as caoutchouc. Despite the varieties of climate to which they were exposed, not one of them would give up the ghost; even the old colonel, who had been twice despaired of, recovered from the yellow fever, and within a week after was lapping his claret at the mess-table as jollily as if nothing had happened.**

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*W. E. Aytoun: The Congress and the Agapedom. Blackwood's Edinburgh Magazine, 1851.

Repeated "Occult" Spinal Subarachnoid Hemorrhage and Spinal Cord Ependymoma

DANIEL E. NIJENSOHN, M.D.*; JAIME LAVENTMAN, M.D.;* ROSS H. MILLER, M.D.*
AND MANUEL R. GOMEZ, M.D.*

An 11-year-old boy had repeated episodes of subarachnoid bleeding during a period of three years. He underwent myelography, aortography, and laminectomy for exploration, but no tumor was found. Subsequently, a thoracic cord ependymoma of grade 3 was found. Spinal subarachnoid hemorrhage may be a significant finding in relation to spinal cord ependymoma.

ALTHOUGH CEREBRAL NEOPLASMS may cause a symptomatic subarachnoid hemorrhage,[1,2] this is an unusual event in cases of spinal cord neoplasms.[3-6] It is even more unusual that massive bleeding from a spinal cord tumor extends to the intracranial subarachnoid space, thus simulating spontaneous intracranial subarachnoid hemorrhage.[7]

The syndrome "spinal subarachnoid hemorrhage,"[8] first described by Fincher[9] in 1951, is characterized by intermittent symptoms of meningeal irritation, severe headache, sciatica, and paralysis or sensory disturbance (or both) in trunk or extremities. The initial symptom is low-back pain. Lumbar puncture reveals bloody cerebrospinal fluid. The source of the bleeding may long remain occult.

The patient reported herein illustrates the difficulty of arriving at the proper diagnosis of spinal cord neoplasm in a patient with intermittent subarachnoid bleeding.

Case Report

An 11-year-old boy of subnormal intelligence was first seen at the Mayo Clinic in May 1963 because of severe lumbosacral pain extending to both lower extremities; the duration of the pain was approximately three weeks. Five weeks earlier, he had fallen off a hayloft, and he also had been kicked by a cow. One week after the onset of pain, examination in his local com-

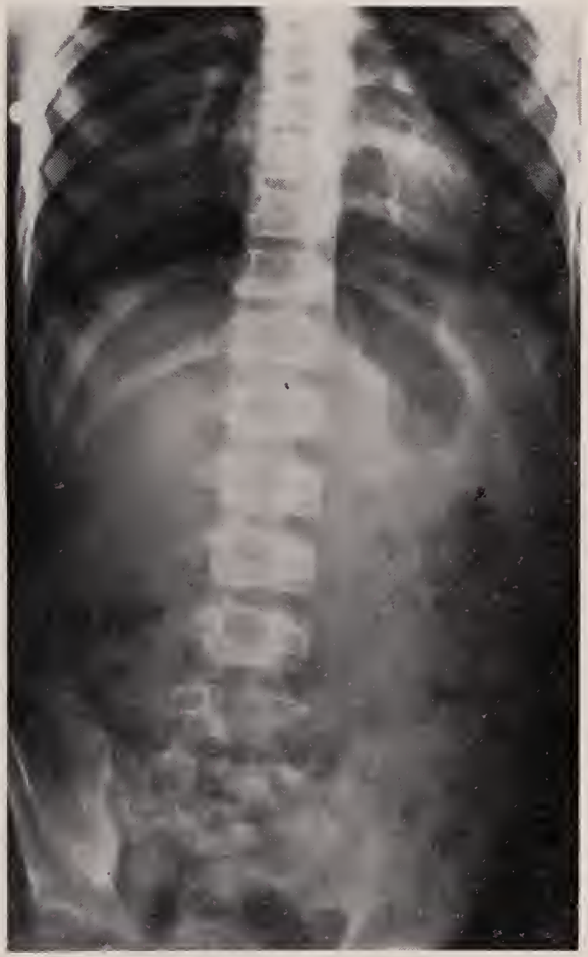

Fig. 1—Roentgenogram on first hospital admission shows no abnormality.

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munity revealed grossly bloody cerebrospinal fluid.

Examination at our clinic disclosed a rigidly straight thoracolumbar spinal column. Movement of the spinal column caused severe back pain. The meningismus extended to the entire column, and tenderness was present in the lumbosacral region. There was generalized hyperreflexia but normal plantar reflexes.

Roentgenograms of the vertebral spinal column showed no abnormalities (Figure 1). Cerebrospinal fluid, obtained by lumbar puncture, contained 1 million erythrocytes. 344 neutrophils, and 200 lymphocytes per mm^3 and 4,300 mg of protein per 100 ml. While under general anesthesia, in preparation for myelography, the patient suffered a severe hypotensive episode and the procedure was cancelled. The patient's back pain slowly improved with physical therapy, and his symptoms were much improved.

Eight months later, he returned to our clinic because of back pain that he experienced for two weeks after a fall in school. He had meningismus of the neck and spasm of paravertebral and hamstring muscles. No bruit could be heard in the head or along the vertebral spinal column. The cerebrospinal fluid was bloody. A myelogram (Pantopaque) was performed. Only one ml of oil was injected at the level of the L-3 interspace, and it outlined many markedly edematous nerve roots in the cauda equina. None of the contrast medium moved, suggesting the presence of an adhesive arachnoiditis. An exploratory bilateral laminectomy from L-1 to L-4 was done. Opening of the dura revealed a marked arachnoiditis. There was no evidence of intraspinal tumor. Biopsy of the arachnoid disclosed acute and subacute inflammatory changes with fibrous thickening and hemosiderin deposition.

Two years five months after the onset of symptoms, the boy had difficulty starting micturition. His back pain had increased, and the pain had extended to both legs. He was unable to walk and had meningismus and flaccid paraparesis, with greater weakness in the distal than in the proximal muscles. Sensation to pain and touch was diminished in his perineal region. There was clinical and electromyographic evidence of lower motor neuron involvement in both lower extremities. A thoracic aortogram disclosed an abnormal spinal artery arising at T-10 (the origin being either the aorta or the 10th intercostal artery) and entering the neural canal and coursing caudally into the region of the conus. Examination of the cerebrospinal fluid demonstrated xanthochromia, 1 lymphocyte and 25,000 erythrocytes per mm.^{3} and 4,770 mg of protein per 100 ml. Fluoroscopy. after a small amount of contrast medium was injected at T-6, revealed evidence of complete obstruction at T-10. The obstruction was attributed to a chronic arachnoiditis. Symptoms subsided after myelography.

Three and one-half years after the onset of symptoms,

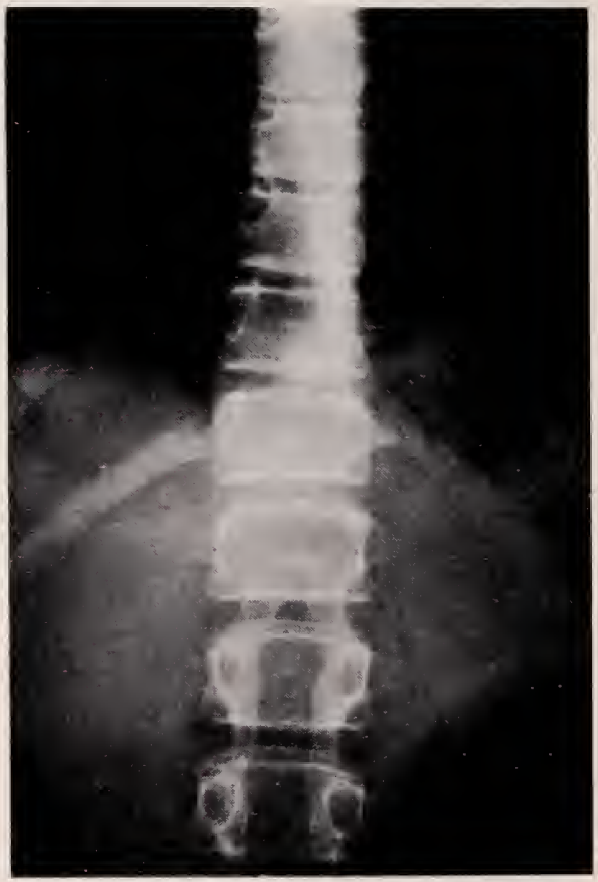
Fig. 2—Roentgenogram of thoracolumbar spinal column shows thinning of pedicles, erosion of T-12 and L-1 bodies, and widening of interpedicular diameter.

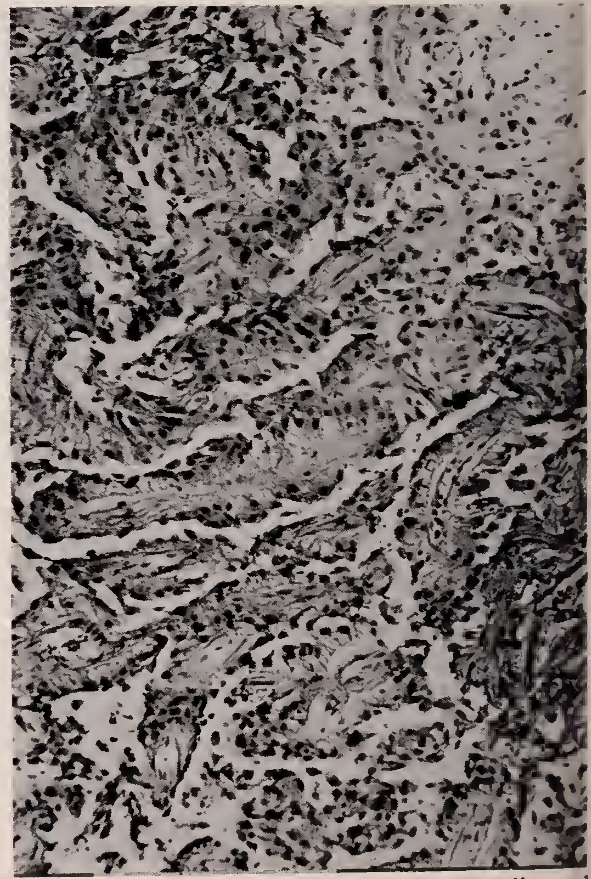
Fig. 3—Grade 3 ependymoma. (Hematoxylin and eosin; enlarged from x100.)

the boy again complained of back pain. Examination revealed severe weakness in the lower extremities (the weakness being greater distally than proximally), muscle atrophy, and absent deep tendon reflexes. The anal sphincter was weak. There was loss of touch, pain, and vibratory modalities of sensation in both lower extremities.

Roentgenograms of the thoracolumbar spinal column demonstrated extensive thinning of the vertebral pedicles, erosion on the posterior aspects of T-12 and L-1 bodies, and wide interpedicular diameter (Figure 2). Tomograms of the lumbar spinal column revealed erosion of the medial aspect of vertebral pedicles and anterior bowing of the posterior aspect of the body of L-1 vertebra. Surgical exploration disclosed a large intramedullary tumor of the thoracolumbar cord extending to the conus medullaris and cauda equina. Microscopic examination demonstrated a grade 3 ependymoma (Figure 3). The tumor was removed subtotally, and radiation therapy was given to the thoraco-lumbo-sacral region.

Although at the last surgical procedure the neoplasm extended from the lower thoracic segments to the conus medullaris and the cauda equina, the tumor was thought to have arisen in the lower thoracic portion of the spinal cord.

Comment

Low-back pain was the patient's first symptom, as in all 15 patients who had subarachnoid hemorrhage associated with spinal cord tumors who were described by Nassar and Correll.[6] Exacerbation of pain with physical activities and trauma was observed in our patient and in five of the 15 patients in the series by Nassar and Correll.[6] Meningismus and intense paraspinal muscle spasm were constant findings on each admission, whereas sensory, motor, and sphincter involvements were late symptoms. There was a persistent elevation of protein level in the cerebrospinal fluid. Although the first myelographic studies demonstrated a subarachnoid block, an exploratory laminectomy failed to disclose the tumor.

Of 169 ependymomas of the spinal cord reviewed by Slooff, Kernohan, and MacCarty,[8] only five were histologically classified as grade 3 and none was classified as grade 4. One of the five grade 3 ependymomas was located in the thoracic region. No patient in their group presented clinically with subarachnoid hemorrhage.

Ependymoma was found in eight of the 15 patients with spinal neoplasms and subarachnoid hemorrhage described by Nassar and Correll.[6] All of the ependymomas and 14 of 15 spinal cord tumors were located in the region of the conus medullaris or filum terminale. According to Russell and associates,[10] ependymomas at this level are not well encapsulated and are formed by a thin connective tissue stroma that contains numerous blood vessels. The biomechanics of the spinal cord during exercise and in different postures explain their tendency to bleed. The bleeding is thought to be of venous origin and to be caused by rupture of congested pial venules during violent physical effort.[8]

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Dr. Chet Anderson

Dr. Chet Anderson, Hector family physician, was honored by the Minnesota Academy of Family Physicians at their annual banquet in April. He was presented the Merit Award for the greatest contribution to family practice in Minnesota in 1973.

Colposcopy

P. P. WILLIAMS, M.D.[*]

Colposcopy is a useful technique that has been neglected too long. Complementing cervical cytology, and based on characteristics of physiologic and pathophysiologic color, contour, and angio-architecture, colposcopy allows an extension of diagnostic acuity otherwise unavailable. The investment is small and the return great, particularly when mutilating procedures can be avoided. In the future, the performance of conization without prior colposcopy may be regarded as a questionable procedure. Whenever a question exists regarding the state of the lower genital tract generally or the cervix specifically, colposcopy must be considered in seeking the answer.

VISUALIZATION OF THE uterine cervix is an important part of any gynecologic examination. Some features are evident; some may or may not be what they appear; others are announced only by abnormal cervical cytology. Diagnostic acuity can be extended beyond the naked eye, without resorting to mutilating procedures, by selective use of the colposcope.

What?

Hinselmann introduced colposcopy in 1925, in an attempt to devise a method for examination of the cervix at a level more refined than naked eye inspection would allow, some 20 years before Papanicolaou's pioneering work[1] in cytology. Implementation in European clinics followed. Until the appearance of Bolten's text,[2] the lack of suitable basic literature in English impeded the spread and acceptance of colposcopy among American physicians. Recent texts[3,4] are superior in quality even to Bolten's.

When colposcopy was first introduced into the United States, pre-malignant conditions of the cervix and carcinoma in situ were poorly understood, and the technique of colposcopy and its applicability were not appreciated. Currently, virtually all major medical centers have at least one trained and active colposcopist. Many of these centers have formally structured operating abnormal cytology or colposcopy clinics.[†] House officers are being trained in colposcopy. Interest is spreading in the private sector. (Much of the current impetus came from individuals primarily involved in private, clinical medicine.[5-7]) Formal courses[‡] are now available and present basics upon which individual experience can build proficiency.

The colposcope itself is a low-power stereoscopic microscope operating outside the vagina at an average focal length of 22 cm. The intense illumination provides an amazing extension of visual acuity with the usual 10x-20x magnification. The instrument is mounted on either a table or a floor stand, and simple hand controls allow for easy adjustment and focusing. A micrometer device is often included within the optics of the instrument and allows measurement of involved areas. A green filter is provided for accentuation of vascular detail. Several available instruments have provision for attachment of a 35 mm camera. Stereoscopic or single-frame colpophotographs may be taken, which are useful in documenting findings and in recording the progression or regression of lesions.

Accessory instruments, equipment, and supplies include assorted vaginal specula, endocervical specula, endocervical curettes, biopsy instruments, Pap smear spatulas, small cotton balls, cotton-tipped applicators, Pap smear fixative, frosted-end microscope slides, specimen bottles containing 70% formalin, a supply of 3% acetic acid solution, and proper recording forms.

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[‡] Information on dates and locations is available from: American Society for Colposcopy and Colpomicroscopy, 701 Dupont Building, Miami, Florida 33131.

See editorial, page 721.

Colposcopy, in its current usage, is complementary to and not competitive with cytology. Either technique alone is only approximately 85% accurate[6,8,9] in the detection of potentially malignant or early malignant cervical epithelium. In combination, 98% accuracy has been claimed.[6,8,9] Regardless of technique, cytologic samples are non-specific. In the face of cytologic abnormality or questionable clinical findings, colposcopy provides a certain specificity. Stereoscopic viewing, with magnification and direct illumination, allows the localization of areas judged to be abnormal on the basis of alterations in color, contour, and angio-architecture. Such localization allows selective cytology or the acquisition of tissue for histologic examination upon which definitive diagnosis depends. On the other hand, visualization with magnification and direct illumination can provide reassurance regarding normalcy.

How?

The patient to be examined colposcopically is positioned on the examining table, as for a pelvic examination. An electrically operated adjustable table is advantageous, but not essential.

The cervix is maximally exposed with an appropriate vaginal speculum. Any questionable vaginal discharge is sampled for later hanging-drop preparations, and appropriate cultures are plated for *N. gonorrheae*. Excess mucus and debris are gently removed with a dry cotton ball. In the Colposcopy Clinic at University of Minnesota Hospitals, a Pap smear is then taken by the cervical scraping technique. Others prefer a combined cervical-vaginal pool specimen[10] or a cervical-endocervical-vaginal pool technique.[11] Kolstad and Stafl[4] favor proceeding next to a systematic evaluation of the cervix, fornices, and vagina so as to appreciate the vascular detail which is more evident prior to application of acetic acid. Most authors[2,3,12] proceed directly to a generous application of 2% or 3% acetic acid in normal saline solution (Hinselmann test). While it serves as a mucolytic, the mechanism of action on the epithelium is uncertain. Within two to three minutes, features important in colposcopic diagnosis become evident. Reapplication may be necessary during the systematic examination of the cervix, fornices, and vagina, as details fade. Depending on certain criteria, the examination is classed as positive, negative, or indecisive.

If negative, no further evaluation is necessary.

If indecisive, other diagnostic methods must be employed as dictated by the original indication.

If positive, colposcopically directed biopsies are taken, specially mounted for purposes of orientation, and submitted, properly labeled, for histologic diagnosis.

It has been stated that colposcopy cannot evaluate the proximally placed squamocolumnar junction.[13] In a minority of cases, this is true; in many, however, all or almost all of the endocervical canal can be visualized with the aid of an endocervical speculum.[14] Endocervical curettage investigates many canals otherwise obscured and is a routine part of initial evaluation in most clinics.

Following completion of tissue sampling, hemostasis is achieved with silver nitrate, ferric chloride solution, or a vaginal tampon. Proper records are completed and findings and plans for follow-up are discussed with the patient. Protocols used at University of Minnesota Hospitals are shown in Tables 1-4.

An initial complete colposcopic examination usually requires 15 to 20 minutes. Follow-up examinations can be completed in less than 10 minutes.

Why?

This question might be approached in one of three ways: "Why perform colposcopy?",

TABLE 1

Protocol for initial visit

1. Patient interview
2. Method of examination:
   - A. Take Pap smear
   - B. Apply 3% acetic acid to cervix
   - C. Examine cervix with colposcope
   - D. Apply Schiller's Test to cervix
   - E. Do selective biopsies
3. Complete colposcopy records and forms
4. Instruct patient to return in two weeks to discuss results

TABLE 2

Protocol for follow-up visit

1. Review interval history with patient
2. Review previous colposcopy forms
3. Method of examination:
   - A. Take Pap smear
   - B. Apply 3% acetic acid to cervix
   - C. Examine cervix with colposcope
   - D. Apply Schiller's Test to cervix
   - E. Do selective biopsies
4. Complete colposcopy records and forms
5. Instruct patient to return to colposcopy clinic as indicated

"Why is colposcopy indicated?", or "Why is colposcopy possible?" Because the first two possibilities lead directly to a discussion of the indications for colposcopy, which will be dealt with in the next section, the concern here will be why colposcopy is possible.

As stated previously, colposcopic detection of abnormalities depends on alterations in color, contour, and angio-architecture of the cervicovaginal epithelium. Understanding why colposcopy is possible is based on understanding how these abnormalities develop.

As is always appropriate, normal development forms a basis for considering abnormal development. The process of somatic sex differentiation in the female begins at about the 10th week of gestation. The müllerian ducts differentiate into the fallopian tubes and uterus. The uterus is derived from the fused caudal portions. While considerable debate exists as to the exact site and mechanism, junction between the epithelia of the urogenital sinus and the caudal müllerian ducts occurs.[15] Vilas[16] and Meyer[17] claimed that it is marked in the adult by the squamo-columnar junction. Koff[18] felt that the junction was in the upper third of the vagina. Fluhmann's review and work[19] led him to believe that the junction was higher and occurred at the internal os.

Regardless of the precise embryological development, it has long been recognized that columnar epithelium is found on the portio of the cervix, even extending onto the upper vagina, in the fetus, the pre-pubertal female, and the pubertal and adult female.[20]

TABLE 3
Protocol for follow-up schedule

1. Initial examination
2. Return examination—two weeks:
   - A. Discuss results of cytology, biopsy and colposcopy with patient
   - B. Outline method of treatment with patient, treat with cryosurgery if indicated
   - C. Schedule follow-up visit
     Clinic procedure for follow-up visit to be followed
     1. Every three months during first year
     2. Every six months from second to fifth year
     3. Every 12 months after five years

TABLE 4
Protocol for treatment

1. Benign findings:
   No treatment; return to colposcopy clinic in three or six months
2. Severe dysplasia, carcinoma in situ, or suspect invasion: schedule cone biopsy
3. Mild or moderate dysplasia, symptomatic ectopy, endocervicitis, etc.: cryosurgery

The process of metaplasia[21] is an inextricable part of the ultimate relationship of squamous and columnar epithelium of the uterine cervix. The colposcopic picture of metaplasia, typical and atypical, accounts for why colposcopy is possible. Metaplasia occurs in the transformation zone; that area lying between the mature or original squamous epithelium and the columnar epithelium. This is a dynamic area, with a tendency toward progressively more mature squamous epithelium in the typical course. The fully mature squamous epithelium found in this area is the result of true metaplasia and not in-growth from surrounding native epithelium, as has been taught for many years.[21,22] Recognition of the potential for variability in the level of junction of the müllerian ducts and the urogenital sinus negates the concept of "erosion," with its attendant "maceration" and "to and fro" concepts.[23] This, in reality, is columnar epithelium.[21,22] Metaplasia, involving this columnar epithelium, produces the adult picture.[21,22] The extent of squamous epithelialization and, similarly, the amount of exposed columnar epithelium seen in the apparent view of the cervix (the appearance of the cervix produced by the open speculum) with or without the colposcope, normally varies widely. Progression, not regression, characterizes the metaplastic process. Under the influence of estrogen and altered vaginal pH, metaplasia is at its peak at puberty and at approximately 12-14 weeks gestation in the first pregnancy.[21,22] Assuming normalcy, the metaplastic squamous epithelium is laid down in an orderly fashion, culminating, albeit variably, in the adult picture.

In those situations where the course is not normal, atypicality characterizes the process and dysplasia begins. The various degrees of dysplasia may progress to carcinoma in situ and finally microinvasive carcinoma.[24] It is felt by some that this change from typical to atypical may be the result of a mutagen.[25] Regardless of the nature of the process, it occurs in the area known to colposcopists as the transformation zone. The changes in color, contour, and angio-architecture of the atypical transformation zone account for why colposcopy is possible.

Imprecise and confusing terminology has constituted another barrier to the acceptance of colposcopy in this country. While detailed discussion of these changes and their genesis is beyond the scope of this paper, the widely used new American terminology is shown in Table 5. This terminology has been accepted by the American Society for Colposcopy and Colpomicroscopy. For a discussion of these changes, the reader is referred to Coppleson et al.[3] and to Kolstad and Stafl.[4]

TABLE 5
New terminology of the American Society for Colposcopy and Colpomicroscopy

A. Normal
   1. Original squamous epithelium
   2. Columnar epithelium
   3. Typical transformation zone
B. Abnormal
   1. Atypical transformation zone
      a. White epithelium
      b. Mosaic
      c. Punctation
      d. Leukoplakia
      e. Atypical vessels
   2. Suspect frank invasive cancer
C. Miscellaneous
   1. Vagino-cervicitis
   2. True erosion
   3. Atrophic epithelium
   4. Condyloma, papilloma, etc.
D. Indecisive (entire squamocolumnar junction not seen)

When?

The remaining unanswered question is, "When is colposcopy indicated?" Several indications have been put forth (Table 6).

TABLE 6
Indications for colposcopy

1. Mass screening
2. The suspicious Pap smear
3. The positive Pap smear
4. The "red, angry cervix"
5. Diagnosis of vaginitis

Ideally, but not practically, colposcopy may be used for mass screening. Ample evidence of its effectiveness in this respect comes from the experience of European centers where it has been employed in this fashion for many years.[26] Cost and time considerations make this approach impractical in most settings in this country.

Because of certain epithelial characteristics produced by the responsible organisms, some types of vaginitis are diagnosable with the colposcope,[27] but to use the instrument primarily in this manner is somewhat akin to hunting flies with an elephant gun. If a diagnosis is made in the course of an examination on another basis, well and good. Hanging-drop and culture techniques are more reliable, less costly, and quicker.

Several "miscellaneous conditions" (Table 7) can be elucidated with the colposcope. Amplification of these conditions is inappropriate here, as their evaluation requires some appreciation of colposcopic nuances.

TABLE 7
Miscellaneous conditions

1. Vagino-cervicitis
2. Atrophic cervicitis
3. True erosion
4. Polyp
5. Condyloma and papilloma
6. Inconspicuous iodine—negative area

The "red, angry cervix" is an excellent candidate for colposcopic examination. As implied above, most "cervical erosions" are not erosions at all, but rather areas of exposed columnar epithelium.[21,22] Frequently these "nasty looking lesions," which may be asymptomatic, are cauterized. It is perhaps appropriate to consider the propriety of two points. Is cautery of the asymptomatic, benign cervix indicated? Should a cervix be cauterized without first being colposcoped? Colposcopy will certainly indicate the situation.

Colposcopy is most useful in the case of the suspicious or positive Pap smear.[3,5,8,28-31] This is generally so. It is even more so, specifically, in that apparently growing group of women who show abnormal cervical cytology in their childbearing years.

Punch biopsy has been advocated in such cases.[32] Some of its inherent randomness is eliminated by the use of Lugol's solution.[33] Any alteration in cellular glycogen content alters iodine uptake, and many histologically benign tissues, including columnar epithelium, fail to stain. Recognition of the statistical distribution of lesions of the cervix[34,35] and consequent abandonment of the classic four-quadrant approach changes things little. Even biopsy of the nonstaining areas[33] of the anterior and posterior lip cannot guarantee that the most abnormal area is sampled. What if the biopsy is nondiagnostic?

Immediate conization in the face of abnormal cytology is another approach.[36,37] Regardless of ease and technique, conization is a mutilating procedure, with potential for immediate and long-term consequences[38] (Table 8). In pregnancy the potential for problems is considerable and the consequences dire.

What about those lesions outside the usual areas considered for punch biopsy or included in a conization? The answer is evident.

TABLE 8

Complications of cervical conization (10% or greater)

1. Hemorrhage
   - A. Immediate
   - B. Delayed
2. Infection
3. Cervical incompetence
4. Cervical stenosis

When faced with abnormal cytology from the lower genital tract, the colposcopist, assuming an adequate examination, can define the extent of many lesions, obtain selective specimens for confirmatory cytology, and selectively biopsy the most abnormal area or areas for definitive histologic diagnosis.[39,40] In selected cases, complete excision can be colposcopically directed.[6,40] In other cases, where conization is truly indicated, the colposcope can provide direction and can even be taken into the operating room. Most importantly, adequate colposcopy can assure benignity and obviate the need for biopsy altogether. The squamocolumnar junction must be seen in its entirety for a colposcopic examination to be considered adequate.

In any cases of proven malignancy managed conservatively, follow-up colposcopy is ideal.

In pregnancy, colposcopic evaluation can allow temporization of even directed biopsy based on a judgment of the quality of any colposcopic abnormality noted.[7,40,41] Coppleson[24,25] and others[42] have drawn reliable correlates between the character, or quality, of colposcopic abnormalities and the histopathologic changes.

The answer to the question, "When is colposcopy indicated?" is "Whenever." Colposcopy is indicated whenever a question exists regarding the state of the lower genital tract generally and the cervix in particular, regardless of whether the question is raised by abnormal cytology or by appearance.

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Recent Advances in the Management of Pain

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Percutaneous and stimulating techniques for pain relief has brought about a resurgence of interest in the physiology on therapy of pain.

THE MANAGEMENT OF pain is an old, and frustrating problem.[2] The treatment of acute pain by using analgesics and eradicating the primary disease is reasonably successful, though narcotics for pain relief introduce unwanted clinical problems. Treatment of chronic pain has been less satisfactory. As the medical management of many diseases has improved, the magnitude of the problem of chronic pain has increased. Improved therapy in paraplegia, trauma, and cancer, has added to the pool of patients suffering from disabling pain. As in acute pain, treatment of the underlying disease is most desirable. But if such therapy is not available, procedures designed purely for pain relief are required.

The first option is the administration of narcotics over a long period of time. The addiction that results may become more serious than the original pain problem. This expedient should be reserved for patients whose survival is likely to be short. Neurotomy or rhizotomy may be employed for pain located in precise areas but carry with them the certainty of neurological deficit. Operative cordotomy for years has been the bulwark of the neurosurgeon's armamentarium for pain relief. Division of the anterolateral spinothalamic tract at the thoracic or cervical level is a reliable procedure which can be performed with a small risk of serious neurological sequalae. However the operation is a major procedure and the risks of neurological loss, though small, are still present. A variety of pain relieving procedures have been performed in the brain, primarily by stereotaxic methods, but most are not reliable enough to be used as primary procedures for permanent pain relief.

Because of these difficulties and shortcomings, new approaches for the relief of pain have been developed. These new avenues of therapy are of two types. First are those in which an old operation, such as cordotomy or retrogasserian rhizotomy for trigeminal neuralgia, have been modified to allow percutaneous, radiofrequency destruction of nervous tissue, thus avoiding a major operation. The techniques are now standard and, their value well established. The second type is based upon the concept of electrical stimulation of non-painful sensory fibers for the suppression of pain sensation. These procedures, are in the stage of investigation and development.

Radiofrequency Percutaneous Cordotomy

In principle, percutaneous cordotomy is exactly the same as the well-known open anterolateral spinothalamic cordotomy. Analgesia is produced without loss of other major sensation and when successful, without loss of motor function. The great advantage is that it can be performed quickly in an awake patient without a major operative procedure. Under fluoroscopic and x-ray control a spinal needle is placed into the second cervical (C_2) neural foramen. Penetration of the cord is verified by special electrical measurement. A radiofrequency generator is used to produce a lesion in the spinal cord. It is often possible to begin by producing analgesia in the desired part of the body, and extend the level to provide relief of pain without completely eliminating sensation

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contralaterally. Unfortunately this close control is not always possible and analgesia to the C_2 level is common and often desirable.[3] When bilateral analgesia is required a special problem exists. If lesions are made in the spinal cord in both anterolateral quadrants in the C_2 level, there is risk to respiratory function.[1] These patients present a characteristic syndrome in which respiratory function is satisfactory when they are awake and alert, but lacking adequate reflex control, their respiration fails at night. This problem may be avoided by creating very small lesions at the C_2 level. It is probably more satisfactory, however, to create the second lesion in the spinal cord via an anterolateral approach through the disc at the $C_{5,6}$ level.

Percutaneous cordotomy can be repeated as necessary and an overall success rate of close to 90% can be attained. Neurological complications are not greatly different from those seen with the open procedure. Motor or sensory loss, bladder dysfunction, impotence, and postural hypotension, are possible complications. These are more common with bilateral lesions. The procedure is quite satisfactory for individuals with a malignancy and life expectancy of less than two years. Beyond two years, the level of analgesia begins to fail and recurrence of pain is common. A small percentage of long term survivals will be left with painful dysesthesias in the denervated part, and these are difficult to treat. Patients with far advanced malignancy can be treated with reasonable safety.[1,3]

Radiofrequency Percutaneous Retrogasserian Rhizotomy

An analogous technique has been devised for the destruction of trigeminal nerve fibers in trigeminal neuralgia. Previously, these patients could be successfully treated by medical therapy, or by peripheral neurotomy, retrogasserian rhizotomy, and occasionally by the division of the fifth cranial nerve in the posterior fossa. Though Tegretol and Dilantin are effective, the side effects of the drugs are many. Peripheral neurotomy is of value in helping only some of these patients, and retrogasserian rhizotomy or posterior fossa division of the fifth nerve leads to sensory loss in the face. Compression of the nerve without division is also effective in relieving pain and spares sensory function, but recurrence of pain is not uncommon. Radiofrequency destruction is a procedure which can be done without a general anesthetic and without a major operation. It usually will provide analgesia without loss of light touch and corneal sensation. The complication rate is small, and if pain recurs the procedure easily can be repeated. Partial destruction of the nerve is accomplished using a radiofrequency lesion generator. The small pain fibers are much more sensitive to heat and therefore can be destroyed differentially, leaving touch more or less intact. Complications of the procedure have primarily been transient loss of motor fifth nerve function and an occasional extraocular muscle paresis, which usually clears promptly. As with percutaneous cordotomy, the procedure has the great advantage of being simple, and can be used in aged and debilitated patients who are all too often those with trigeminal neuralgia.[5]

Control of Pain by Electrostimulation

The current applications of electrical stimulation for the relief of pain are of three types. The first requires external attachment of electrodes and stimulation by an electrical current delivered to the skin or through the skin. The second technique entails stimulation of spinal cord or peripheral nerves, either transcutaneously on a temporary basis, or via implanted electrodes. The third, which is now under development, is stimulation of various areas within the brain for the control of pain.

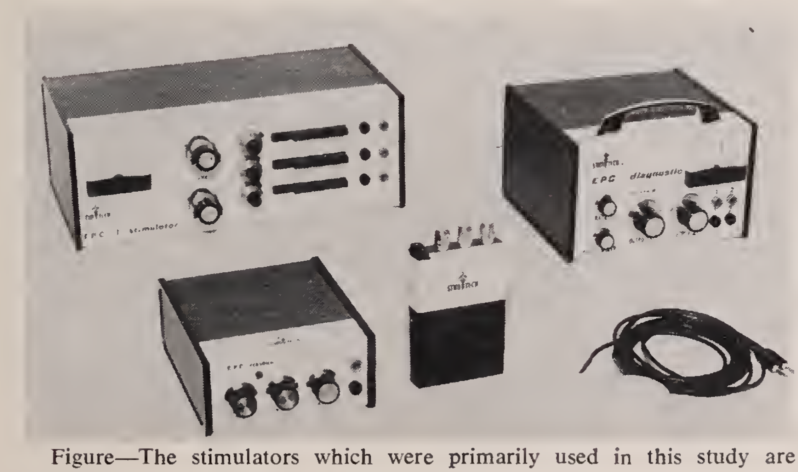
External Stimulation

The principles of external stimulation for the control of pain are well known, and a variety of stimulators are available. Many types of pain can be effectively controlled on a short-term or long-term basis by the simple expedient of external electrical stimulation. The reliability of the device as a screen for those patients who would benefit from permanently implanted stimulating devices has also been good. The electrical characteristics of the majority of these and certain drawbacks of design made them less than satisfactory. New designs have greatly improved external stimulation techniques. The instrument with which we have had the greatest experience is the EPC I manufactured by the Stimtech Corporation (Figure). We also have had experience with a model currently being developed by the Medtronics Corporation. These devices provide control of voltage, frequency, and characteristics of the electrical pulse. The voltage output of the machines is high, but the current flow is extremely low so that they are not dangerous. Their use is not recommended in patients with serious myocardial disease, though as yet we do not have data that suggests they would be dangerous for such patients. The electrodes are applied in or near the painful area and stimulation and position are varied until pain relief is adequate. Most of the patients that have been so treated have suffered from the chronic low back syndrome, often have had multiple operations, and rarely have been helped by any standard methods of pain control. Relief is often dramatic and complete. It usually is maintained as long as the stimulation is continued. A few fortunate patients have a prolonged after-affect from the stimulation though in the majority the pain returned as soon as the sensation of stimulation disappears.

External stimulation has been used primarily in screening patients who are possible candidates for implanted stimulators. The correlation between the response for external stimulation and the response for dorsal column or peripheral nerve stimulation has been reasonably good and currently all patients must show a significant benefit from external stimulation before being considered for an internal implant. Many patients with chronic low back syndrome have responded favorably and patients with stump pain and phantom pain have also been responsive to the treatments. The response of postherpetic neuralgia is less predictable but some of these patients are dramatically relieved. These devices have also been used successfully in acute postoperative pain for obstetrical analgesia, and in acute and chronic cervical syndromes. Tension headaches, arthritic pain, and minor athletic injuries have also responded. The number of patients treated in all of these areas has not been large.

The use of external stimulation as a diagnostic and therapeutic agent appears very promising. It certainly seems that a large number of relatively minor painful states can be controlled quickly and effectively using the stimulating devices. External stimulation provides a reliable diagnostic screen for patients who may benefit from an internally implanted device. The instruments are small, portable, and the patient can easily perform the stimulation at home. Many patients initially thought to be candidates for implanted stimulators find that the periodic use of the external device makes life tolerable for them, and no further procedures have been required. The patient must be thoroughly instructed in the use of the instrument. It takes several days of trial application in various areas to establish where the electrodes should be located and the amount of stimulation that should be used.

Complications are minimal. There have been a few patients with tape allergy where fixing the electrodes became a problem, a few people have



Figure—The stimulators which were primarily used in this study are pictured above. The prototype is at the right: a hospital stimulator is at left: two personal models and standard electrodes are in the foreground.

sustained minor electrical burns or allergic reaction to the electrode material. Hysterical, psychotic or severely neurotic patients may say the stimulator worsens their symptomatology, and often describe bizarre effects of stimulation. These patients predictably do not obtain benefits.

Spinal Cord and Peripheral Nerve Stimulation

The concept of electrical stimulation directly applied to the nervous system for pain relief was first given trial by Shealy. Working with the Medtronics Corporation, he has devised a series of electrical stimulators for peripheral nerves and spinal cord.[4] These stimulators activate large afferent fibers which are non-pain carrying and the resultant tingling or buzzing sensation that the patient feels masks the pain. The location of the blockade of pain is not fully understood. The first work in stimulation was based on the concept of a blockade in or near the dorsal root entry zone of the spinal cord.

At the University of Minnesota the procedure for evaluating a patient who complains of intractable pain for the possibility of a dorsal column or peripheral implant is relatively standard. The first step is review of the patient's history, which usually is quite complicated and long, and to assure that there is no further primary treatment for the problem causing the pain or standard and simple pain relieving procedure which is likely to be effective. Each patient then undergoes a psychiatric interview and psychometric evaluation. The presence of reactive depression or anxiety so commonly associated with chronic pain states is no bar to these procedures, but overt psychopathy or hysteria are contraindications. If the patient is felt to be a reasonable candidate for the procedure, a trial of external cutaneous stimulation is undertaken. If the patient responds well to this and the pain is significantly relieved, the stimulation is usually continued for a period of time on an outpatient basis while the patient adjusts to the sensation and decides whether or not the relief afforded by cutaneous stimulation is adequate. Good response to external stimulation suggests but of course does not guarantee that a spinal cord stimulator will be beneficial. If the external stimulation proves cumbersome, or if the patient feels that the pain relief is helpful but not entirely satisfactory, an internal implant either on peripheral nerves or on the spinal cord may be indicated. If the results of external stimulation are indeterminate, further stimulation procedures can be utilized to evaluate the patient. It is possible that stimulation of peripheral nerves transcutaneously may relieve pain not affected by cutaneous stimulation. The posterior columns of the spinal cord can be stimulated by electrodes placed in the subarachnoid space or by actual exploration of the columns by fine electrodes. Relief of pain by any of these techniques suggests an implanted stimulator will be successful. The internal portion of the device is somewhat similar to the cardiac pacemaker. The electrode is a small flat plate of silicone rubber in which a platinum wire is imbedded. The wire is attached to a radio receiver which is implanted subcutaneously, a major operation under general anaesthesia. The external portion of the stimulating device has internal controls which can be pre-set. Some patients require stimulation at all times for adequate relief of pain. Others are able to relieve the pain by short periods of stimulation with prolonged pain relief.

Dorsal column stimulation has been used primarily for patients who are not candidates for any other kind of pain relief and who represent the most difficult problems. Most have had chronic low back pain, they had multiple operations including spinal fusions, and often complications, with infections and pseudoarthroses and arachnoiditis. These devices have also been used in phantom limb and stump pain, postspinal cord injury dysesthesias, and pain from rheumatoid arthritis, injuries to major peripheral nerves and cancer. Currently we employ the dorsal column stimulator for those patients with neoplasms under control with bilateral intractable pain who are otherwise ambulatory and quite functional.

The experience at the University of Minnesota indicates that about 40% of the patients treated will obtain good relief and will become functional individuals again. Another 30% will be benefited, but will retain major disabilities secondary to their neurological losses or to situational problems, such as drug dependency. About 30% will not obtain any relief. The majority of these fail to be helped because of inadequate stimulation related to nervous system injury, electrode placement, or electrical failure. These problems usually can be solved. Few patients have had good stimulation in the area of pain without significant pain relief. Most of our patients have had pain for five to ten years; the number of operations usually exceeds five, and almost all are dependent upon narcotics. The success rate of about 70% is promising.

The complications of any such procedure are important. Exposure of the spinal cord and placement of the device over it may lead to cord injury. Cord compression warranting removal of the device occurred once. The patient however refused to have the electrode removed, stating that her pain relief was so satisfactory that she did not wish to give it up, even at the cost of a neurological deficit. The most common complication has been leak of cerebrospinal fluid around the electrode into the subcutaneous pocket. This usually responds to aspiration. Infection is an obvious complication, reaction to the silastic material may occasionally occur, and electrical failure is possible though rare.

Brain Stimulation

The success of peripheral and spinal cord stimulation for pain relief led to the hypothesis that stimulation within the brain might be more selective and equally effective. It has been known for some time that stimulation in various lower animals will modify their response to pain. The Medtronics Corporation is currently developing electrodes for human thalamic implantation. These devices are similar in principle and design to the dorsal column stimulator, and will be entirely contained beneath the skin. The activating device and power supply will be in the control of the patient externally. A few preliminary reports indicate that this type of stimulation might have great efficacy in such painful states as anesthesia dolorosa, thalamic pain, pain of paraplegia or spinal cord injury and post-brain stem infarction pain.

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Cover Painting

“Coffee Time”

Dr. Clayton M. Ingham, a dentist practicing in Mahtomedi for 26 years, was displaying several of his paintings at the Open Air Art Show on Lake Street in Minneapolis last year. Dr. Stiegler, our art editor, saw the painting and decided immediately that this dentist’s work should illuminate the cover of this hunting season issue of MINNESOTA MEDICINE.

Painting is Dr. Ingham’s hobby. He displays his works at many art fairs. His topics center around sports and oils and acrylics are used. Dr. Ingham is active in many state and national dental associations.

Annual Meeting

The Minnesota State Medical Association’s annual meeting in St. Paul, May 21-23, 1975, at the St. Paul Hilton Hotel.

Transient Global Amnesia

FREDERICK M. VINCENT, M.D.* AND YOUSIF I. HAMATI, M.D.*

Transient loss of memory may be due to definite organic states such as head injuries,[1] epilepsy,[2-3] migraine,[4-6] encephalitis,[5,7] and cerebrovascular accidents.[5,8-12] Transient loss of memory without loss of consciousness has been considered to be of hysterical origin.[13] In 1964 Fisher and Adams described a syndrome presumed to be due to cerebral vascular disease and distinguished from amnesic attacks of psychogenic origin by its occurrence in middle aged patients of stable personality; they termed this syndrome transient global amnesia.[8]

Transient global amnesia is characterized by an attack which is sudden in onset and presents the following symptoms: disorientation in time, confusion, isolated recent memory defect with varying degrees of retrograde amnesia, inability to retain newly presented material, and gradual clearing.[8,14-15] The clinical picture is dominated by amnesia with no other neurological abnormalities during or after the attack.[8,14-15]

Since 1964 several articles on this subject have emphasized that isolated attacks are the rule.[5-6,8-11,16] It has been suggested that transient global amnesia may result from damage to both temporal lobes, probably on a vascular basis affecting the hippocampal-fornical-mammillary body system.[2,5,10-11,17]

It is the purpose of this paper to discuss the differential diagnosis of transient amnesia and to present two case reports.

Case Reports

Case 1

A 67-year-old white male was admitted to St. Luke's Hospital on February 1, 1974, with the chief complaint of loss of memory. On the day of admission he left home to go shopping at 11:30 a.m. The next thing he remembered was at 7:30 p.m. that evening. The following events were pieced together by members of the patient's family. After leaving home, he drove to the bank and withdrew money to pay bills. He then drove to a hardware store, bought a snow rake and returned home where for a two hour period he raked snow off his garage roof. During this time, he talked with a neighbor and he reportedly did not seem to be confused or disoriented. Finishing outdoors, he went inside and talked to his daughter on the telephone at about 4:30 p.m. She thought that he sounded confused so she called her brother and he drove to his father's house. When he arrived, the patient was oriented to place and person, but not to time. He was quiet but vague, seemed fairly alert but could not remember the day's events. His poor recent memory was illustrated by the fact that he did not recognize a bedroom that he had been redecorating for the past six months, and he wondered who was doing that work. His memory span was short, and questions had to be repeated to him many times, e.g., he asked his son about twenty times why he was packing his suitcase. During this episode, the patient had no complaints of vertigo, headache, dysarthria, visual disturbances, paresis, paralysis, or numbness.

On admission, the patient was noted to have a blood pressure of 165/110. No physical or neurological abnormalities were noted. From 7:30 p.m. on that day, the patient became able to retain new materials, but his amnesia persisted for the preceding events of the day. The patient had a negative past medical history, was receiving no medications, and had no history of significant alcoholic intake. Neuropsychiatric examination was normal, except for the 8.5 hour amnesic period. Complete blood count, urinalysis, blood chemistry profile, and electrolytes were within normal limits. Lumbar puncture revealed clear CSF with normal pressures, a protein of 43mg/100ml and no cells. Chest and skull roentgenograms, electrocardiogram, brain scan, and electroencephalogram were also within normal limits. Cervical spine roentgenograms revealed evidence of mild degenerative osteoarthritis with some posterior lipping and joint space narrowing present.

The patient was placed on anticoagulant therapy while hospitalized, and he had no further attacks of amnesia or confusion and he became normotensive. He was discharged nine days after his admission and has done well to date.

Case 2

A 55-year-old married white female was first seen at St. Luke's Hospital in 1961 with typical symptoms of a subarachnoid hemorrhage secondary to a ruptured aneurysm in the region of the left posterior communicating artery. She had a long history of arterial hypertension. Rupture of the aneurysm was preceded by a long period of left facial pain. Lumbar puncture confirmed the hemorrhage and arteriography localized the lesion. Craniotomy with ligation of the aneurysm was carried out, and post operatively the patient did well except for the development of a right homonymous hemianopsia and an incomplete third nerve palsy. The patient had been in good health since her discharge from the hospital in 1961 and was normotensive from that time.

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On March 23, 1974, the patient was admitted to the hospital with a complete and sudden loss of recent memory that began the morning of admission. At 11:00 a.m. she asked her husband what she had been doing that morning. She could not remember such activities as bundling newspapers, walking to her friend's house to drink coffee, nor could she remember that her husband was recuperating from a recent myocardial infarction. She did not remember going to her physician's office that afternoon, nor did she recall being admitted to the hospital. She was confused as to time, place and detail, but not to person. Between 6 p.m. and 8 p.m. her memory gradually began to return, but she was still amnesic for the events of the day. During this episode of amnesia the patient did not complain of pain, headache, vertigo, visual disturbance, speech difficulties, or hearing defects.

Physical and neurological examinations were within normal limits except for a persistent right homonymous hemianopsia that was described as being grossly unchanged since 1961. Blood chemistry profile, urinalysis, complete blood count, and electrolytes were within normal limits. Lumbar puncture revealed clear CSF with normal opening and closing pressures, protein 43mg/100ml, glucose 59mg/100ml, and 1 wbc per mm^3. Chest roentgenogram, electroencephalogram, electrocardiogram, and brain scan were negative. Skull roentgenograms were negative except for evidence of the previous left craniotomy. The patient refused arteriography.

She did well during hospitalization with no further episodes of amnesia and was discharged five days after admission.

Discussion

There have been a number of articles in the recent literature dealing with groups of patients who presented with transient loss of memory. Transient global amnesia seems to have been the most common cause.[2,5] It must be differentiated from temporal lobe epilepsy, temporal lobe encephalitis, pre-migraine aura, and amnesia secondary to psychogenic causes.[5]

Transient global amnesia usually manifests the characteristics listed in the Table. Most episodes have been single,[8] although multiple occurrences have been reported.[2,5,11,18] Attacks have been associated with taking hot baths,[6] exposure to cold,[5,16] heavy physical exercise,[6] and sexual intercourse.[8]

Temporal lobe epilepsy has been shown to be a cause of transient amnesia, but the patient is usually younger. Episodes tend to be of shorter duration and the EEG is frequently diagnostic.[2,8,19] In the transient amnesia of temporal lobe epilepsy, behavior may be normal but afterward the patient is found to have failed to register the events leading into an apparent seizure.[3,5] Automatisms, depersonalization, and other abnormalities of behavior frequently occur, and when present these features help us to distinguish temporal lobe epilepsy from transient global amnesia.[3,5] Temporal lobe epileptic seizures are not characterized by repetitive questioning and pure recent memory defect as is global amnesia.[20]

Episodes of amnesia have occurred as a manifestation of migraine.[4,5] These cases are rare, but might be expected to be more common in patients with basilar migraine, since both posterior circulations could be affected.[4]

Croft et al.[5] reported two young patients who experienced transient amnesia during a bout of temporal lobe encephalitis, and each patient developed a prolonged amnesic state during the course of his illness when both temporal lobes were damaged by the encephalitic process, as shown by EEG. Later both had attacks of transient amnesia due to temporal lobe seizures.

Psychogenic transient amnesia is usually a conversion syndrome occurring in a patient with a history of hysterical personality disorder. Kennedy and Nelville[13] considered that the cause was often a form of escape mechanism, and some of their patients were reported to be suffering from an intolerable depressive or anxiety state by which escape was secured by loss of memory, loss of identity, disorientation, or a combination of these.[5] When psychogenic factors predominate, the underlying element is usually social.[21] Hysterical fugues end abruptly with a sudden awareness of a long period of time for which there is no memory.[2] In transient global amnesia the retrograde amnesia usually shortens and when recovery is complete the amnesia persists for only the period of the attack itself.[8,12] Attacks of psychogenic amnesia are characterized by the patients' indifference whereas patients with organic memory loss may complain of their defective memory at the time and repeatedly ask

TABLE

Characteristics of Transient Global Amnesia

—patients usually > 50 years
—sudden onset
—no memory of events during attack
—perception and personal identity unaffected
—varying degrees of retrograde amnesia
—patient of stable nature
—no history of epilepsy or psychogenic disorders

questions which demonstrate its severity.[5,8]

Many authors feel that transient global amnesia is a vascular phenomenon, probably resulting from disease in the vertebral-basilar arterial system.[10-11,17,22] Because the clinical picture is dominated by amnesia, many investigators place the lesion in the limbic system.[10-11,17] The role of the hippocampus in the process of memory has been extensively investigated.[23-24,31,33] Amnesia has followed bilateral hippocampal lesions,[26] or unilateral temporal lobe lesions in which the other temporal lobe was the site of some preexisting pathology.[27] Evidence has also shown that medial dorsal thalamic nuclei have been involved in attacks of loss of memory.[11,22] It is well known and documented that infarction of the hippocampi can result in cerebral amnesia.[23-24,28-29]

Tolosa and Gumnit reported recently on two patients with transient global amnesia.[17] Arteriography of one patient showed occlusion of both posterior cerebral arteries. Their evidence points strongly to ischemia in the posterior circulation as a cause of the syndrome. Shuttleworth recently presented two cases of transient global amnesia suggesting cerebral embolus as a cause of the dysfunction.[10]

We believe that both of our patients suffered from transient global amnesia secondary to ischemia in the vertebral-basilar arterial system. Patient #1 had been undergoing strenous physical activity in rather cold weather. Because of osteoarthritic changes in his cervical spine and the fact that he hyperextended his neck for a two hour period, we postulate that there was decreased flow through the posterior circulation, and ischemia to both temporal lobes resulted. Patient #2 has a documented lesion in one temporal lobe, and we feel that she most likely had an ischemic attack that affected the opposite temporal lobe resulting in transient global amnesia.

Some authors believe that transient globa amnesia is epileptic in nature because of the reversibility of attacks, and their similarity to temporal lobe epilepsy.[8,14] However, Jaffe was able partially to test the hypothesis of an epileptic mechanism by administering Valium intravenously to one patient during an attack of transien global amnesia.[30] The patient became drowsy and showed intensification of his disturbance in memory as well as disorientation, contrary to the improvement seen in patients with psychomotor status epilepticus. Jaffe felt that this is good evidence against an epileptic mechanism.[30] I has been suggested that nasopharyngeal recordings during EEG may give better information regarding the state of the mesial temporal lobes.[3

Summary

Two cases of transient global amnesia have been described. In both we postulate ischemia to both temporal lobes with inactivation of the hippocampi. Patient #1 hyperextended his neck for a two hour period while doing strenuous physical activity in cold weather. We believe that these factors, combined with the osteoarthritic cervical spine, resulted in decreased flow through the posterior circulation, and ischemia to both temporal lobes resulted. Patient #2 most likely has infarction of the left temporal lobe, and ischemia of the right lobe would result in inactivation of the hippocampal-formical-mammillary body system. The differential diagnosis of transient loss of memory has been discussed. Transient global amnesia is a characteristic syndrome that can be readily differentiated from the other causes of transient amnesia.

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20-23. See page 714.

Refrigerated Skin Grafts

DAVID W. FLORENCE, M.D.*

With the increase in severe extremity trauma, surgeons are finding an increased need for repeated skin grafting procedures. Adequate split thickness skin, taken at one surgical sitting, properly prepared and refrigerator, can be used for numerous applications on the ward or in surgery, without the need for additional anesthesia.

WITH THE INCREASE in trauma in all age groups, the surgeon is increasingly faced with the problem of loss of skin secondary to lacerations, avulsions, severe abrasions or crushing injuries. The skin loss may be apparent at the time of the injury, or it may be two or three days before the lack of blood supply to the underlying tissues is apparent. The use of skin grafts, therefore, is on the rise; and with the present shortage of plastic surgeons, it is frequently necessary for the general surgeon to solve the problem himself.

Once it has become apparent that a skin graft is necessary, the patient is taken to the operating room. Usually under general anesthesia, the appropriate split thickness skin graft is taken from the predesignated site. In case of lower extremity work, I prefer to use the opposite or uninjured thigh, bearing in mind the possibility of complications to the injured extremity which might result in amputation. If such would be the problem, then using a prosthesis over a previous donor site could produce some problems.

A split thickness skin graft is obtained with whatever instrument the operating surgeon likes. I suggest obtaining twice as much split thickness skin as ordinarily taken to cover the recipient site. The donor site is then treated by the application of two layers of Furacin gauze reinforced with dressing and an appropriate holding bandage.

The recipient site, after being properly prepared for the grafts, is meticulously covered with split thickness skin, sutured around the periphery with continuous or interrupted fine sutures, and appropriate pie-crust openings made on the surface of the graft if bleeding beneath the graft is not controllable at the time of surgery. The recipient site is then covered with moist pieces of cotton if a crater is present or two layers of Furacin gauze if the graft is flush with the surrounding skin level. The important factor is adequate uniform pressure with immobilization being necessary if the graft is in the vicinity of a joint or moving part.

The excess amount of skin which was not used at the initial grafting is then placed in a sterile Petri dish with approximately ten drops of sterile normal saline, sealed with tape and refrigerated (not frozen).

Following the operation, the Petri dish is sealed with masking tape producing a relatively air-tight situation.

The following day all dressings except the two layers of Furacin gauze should be removed from the donor site. When the Furacin gauze falls off of its own accord, then the donor site is healed. Trimming of the loose edges of the gauze on a daily basis may or may not be necessary. Once the gauze is completely fallen from the healed donor site, then the application of a lanolin-containing lotion twice a day is recommended until healthy, mature skin has developed. This prevents the newly formed skin from cracking.

The recipient site should be uncovered completely in approximately three to five days from the time of the surgery depending upon the size of the defect and the thickness of the involved graft. When the initial dressings are removed, the new skin is carefully inspected and any accumulations of purulent material or serum should be decompressed with cotton applicators. The graft is then left open, protected by either a cast, a cradle, or some similar device to keep extrinsic pressure from the graft.

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*Minneapolis, Minnesota.

Within five to six days from the time of the initial surgery, it should be apparent whether portions or all of the graft have either taken or been rejected by the underlying tissues. As soon as it is apparent that a portion of the graft is not viable then a local debridement is done and the area regrafted using a portion of the refrigerated skin. This procedure can usually be done in the patient's room except in the case of smaller children where lack of cooperation may require general anesthesia. Additional donor sites are usually not necessary.

The debridement is usually painless to the patient because of the lack of sensory fibers involved in the denuded area. After local debridement and cleansing with hydrogen peroxide, additional pieces of the split thickness graft may be applied to the denuded area without being sutured in place. The remaining portion of the split thickness skin is returned to the Petri dish, sealed and refrigerated. This procedure may be repeated four or five times without returning the patient to the operating room; and although it may be necessary to apply additional grafts to various areas of the recipient site, this can be done with no more difficulty than found with a wound debridement.

The end result is usually very satisfactory and economical since repeated operating room charges are unnecessary. As to the length of time over which the donor skin remains viable, I can only state that in one case a satisfactory "take" was obtained with the application of skin refrigerated five weeks. This method is simple and can be used by all physicians who treat surgical wounds.

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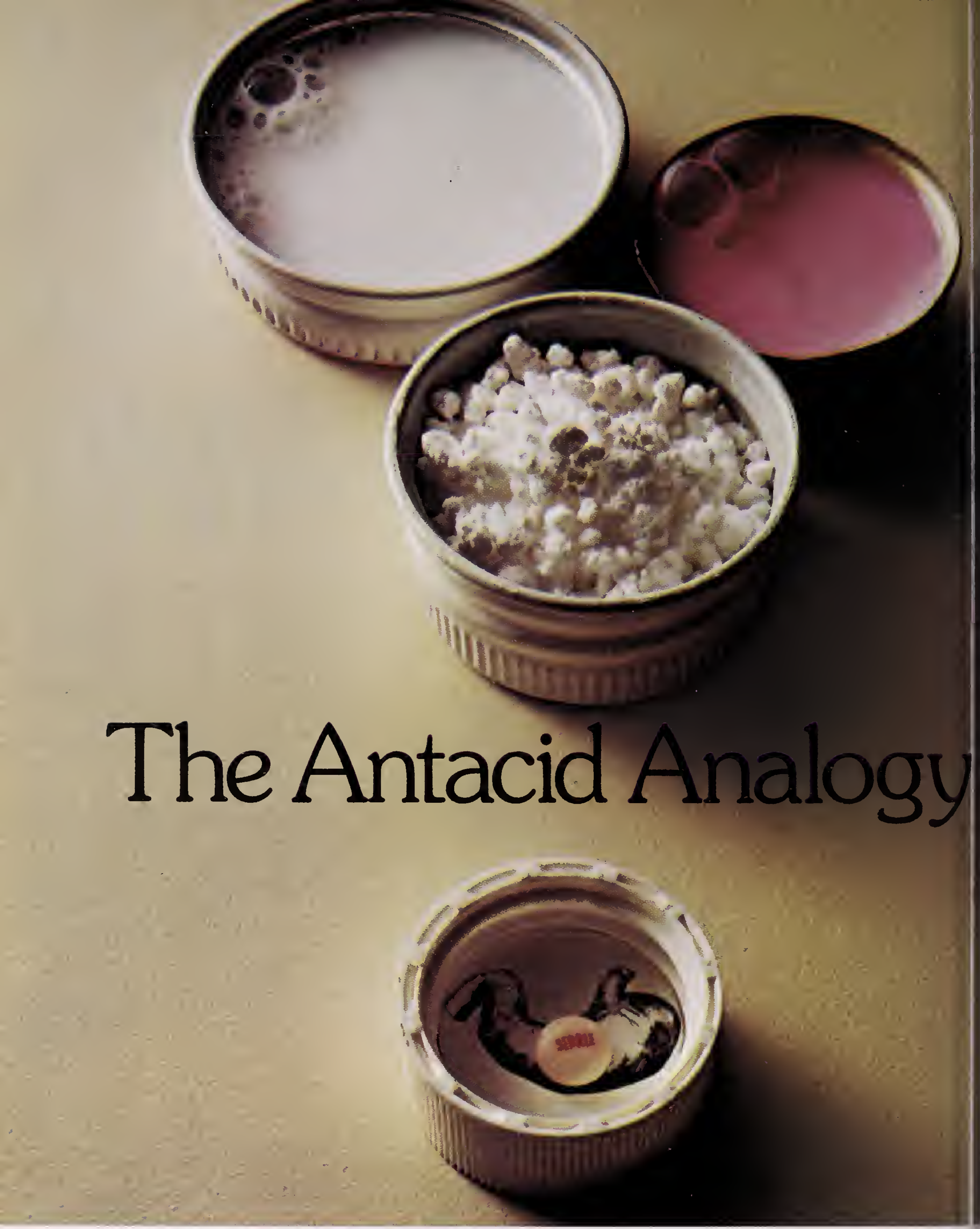

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s well as mydriasis and blurred vision. In addition the following reactions have been reported: nervousness, drowsiness, dizziness, ia, headache, loss of the sense of taste, nausea, vomiting, constipa- potence and allergic dermatitis.

e and Administration: The recommended daily dosage for adult rapy is one 15-mg. tablet with meals and two at bedtime. Subse- adjustment to the patient's requirements and tolerance must be

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Opinion & Dialogue

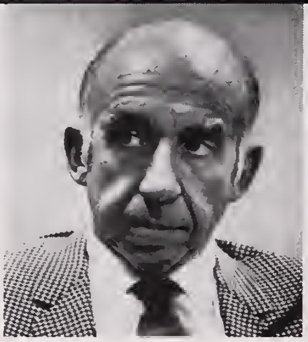
The Role of the Detail Man

Dr. Willard Gobbell
Family Physician
Encino, California

"I may be prejudiced, but I very much in favor of the detail I meet. Most of them are knowlec able about the drugs they promo and can be a great help in acqua ing me with new medication."

Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the years I have gotten to know most the men who visit me regularly a they in turn have become aware my particular interests and the n ture of my practice. They, therefore, limit their discussion as mu as possible to the areas of intere to me. Since I usually see the san representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.



Dr. Jeremiah Stamler
Chairman
Department of Community Health and Preventive Medicine, and Dingman Professor of Cardiology
Northwestern University Medical School

"In the total picture of deali with health problems in this cour there is a potential for detail mer to play a meaningful role."

The Positive Influence

My contact with representa tives and salesmen of the pharma ceutical industry is the type of co tact that people in a medical cent research people, and academic people have and that's in all likeli on a somewhat different level fro that of the practicing physician.

Let me touch on how I perso ally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be — and at times actually are — dissemina tors of useful information. They could consistently serve a real ed cational function in their ability t discuss their products.

At present they do distribut printed material, brochures and pamphlets — some of it scientific ally sound and therefore truly use ful — as well as some excellent fil produced by the pharmaceutical industry. When they function in t

a Source of Information?

Yes, with certain reservations. average sales representative a great fund of information it the drug products he is re- sible for. He is usually able to er most questions fully and igently. He can also supply nts of articles that contain a deal of information. Here, exercise some caution. I usu- ccept most of the statements opinions that I find in the rs and studies which come the larger teaching facilities. s without saying that a physi- should also rely on other es for his information on macology.

ing of Sales Representatives

Ideally, a candidate for the on as a sales representative harmaceutical company d be a graduate pharmacist has a questioning mind. I don't this is possible in every case, o it becomes the responsibility of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

city they are indeed useful; ularly in the fact that they minate broadly based educa- material and serve not just ushers" of their drugs.

ther Side of the Coin

Obviously, the pharmaceuti- mpanies are not producing all aterial as a labor of love— re in the business of selling cts for profit. In this regard nbitious and improperly moti- sales representative can a negative influence on the cing physician, both by pre- g a one-sided picture of his ct, and by encouraging the tioner to depend too heavily gs for his total therapy. In ways, the salesman has often ted objective reality and mined his potential role as an tor.

dustry Responsibility

Since the detail man must be rmation resource as well as esentative of his particular aceutical company, he d be carefully selected and thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.*, the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that information must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

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Editorials

Colposcopy

Doctor Williams' article* on colposcopy is a timely reminder of the vicissitudes of medical care and of the fact that changes and additions to our diagnostic and therapeutic armamentarium are reasonable, proper, and to be expected. Although, over the past 40 years, physicians have been frustratingly slow to accept colposcopy and have even denied its value, this diagnostic procedure is now established, accepted, and—in many instances—indicated. Colposcopy has revealed a new area of tissue architecture, enhanced the clinical correlation of tissue patterns and histopathology, and contributed toward a better understanding of the normal maturation patterns of the cervix.

Colposcopic examination has two important practical advantages. First, any cervix that appears abnormal to the naked eye should be further evaluated by colposcopy to define any lesion that may be present. Second, through colposcopic screening of all patients with an abnormal Pap smear, the use of more costly and more mutilating procedures, such as conization and random biopsies, can often be avoided.

The cost of most colposcopes is under $3,000. An experienced colposcopist can often complete an adequate examination in five to 10 minutes, and the yield in diagnostic accuracy and direction toward therapy is significant and rewarding.

Edward O. Jorgensen, M.D.
Mayo Clinic and Mayo Foundation
Rochester, Minnesota

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*See page 700.

Relief of Pain

As implied in Doctor Long's* article, the traditional neurosurgical procedures for pain relief are based on neuroanatomy, and utilize techniques for destruction of nerve tissue at some point in the pain pathway. A recent trend has been away from destructive procedures and toward a more functional approach, exemplified by the use of electrical stimulation of the skin, peripheral nerves, spinal cord or the thalamus in attempts to modify the transmission and appreciation of pain. Clinical and laboratory investigation of these nondestructive techniques is under way at the Mayo Medical Institutions, and while the neurophysiological basis for pain relief remains to be fully elucidated, there is no question as to the practical value of such methods in a surprisingly large number of pain syndromes.

Edward R. Laws, Jr., M.D.
Mayo Clinic
Department of Neurosurgery

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*See page 705.

Prediction of the Respiratory Distress Syndrome

THE ARTICLE BY Rehm, et al.* demonstrates the usefulness of cord blood serum total protein determination as a tool in early prediction of the respiratory distress syndrome.

To the physician in a small hospital who lives in an age of rising medical costs and sophisticated medical techniques, any reliable predictive parameter which would be helpful in the early selection of infants for transfer to a Regional Neonatal Intensive Care Unit would certainly be looked upon as a great asset.

Rehm, in his study of 543 infants, indicated that infants with cord serum total protein of 4.2 gm/100 cc. or less have about an 80% risk of developing the IRDS, irrespective of gestational age or birth weight. In another larger series involving 2200 infants, the risks would seem to be closer to 50%. At any rate, these figures are statistically significant and only larger studies will give us a more exacting risk figure. Equally as important in this study and others is the reliability of this test using the TS meter. Not only has it been found very reliable, but it is simple inexpensive and can be done with ease by genera laboratory personnel in a matter of minutes.

In recent years, a number of tests have been investigated as possible predictive tools for this clinical state. Alpha -1 anti tripsin has received much publicity, but as the authors point out, i may not have as much predictive value as previous studies seem to have suggested. Over and above this, the test is expensive, time consuming, and requires a more sophisticated laboratory capable of immuno-diffusion techniques.

The small hospital physician who is faced frequently with the possible transfer of the small asymptomatic infant has to rely on a number of parameters in making his decisions—i.e. maternal obstetric history, birth weight, gestational age. cost, etc. Any routine, reliable, expedient, simple and inexpensive test such as this, which would make that decision less difficult, could certainly be an aid. Further investigation should bear this out.

Neal R. Olson, M.D
Olmsted Medical Group, P.A.
Rochester, Minnesota

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*Rehm RD et al.: Prediction of the respiratory distress syndrome. Minnesota Med 57:6:443, 1974.

Serum Creatine Phosphokinase

CLINICAL FAILURE to recognize myocardial infarction remains a problem, despite modern diagnostic methods. Elevation of the serum creatine phophokinase is a widely used sign of myocardial necrosis. The usefulness of this laboratory test is diminshed after surgery, because the operation itself is always followed by elevation of the serum CPK, regardless of the site or extent of the surgical procedure. This disguises elevation of CPK caused by ischemic myocardial damage.

A study of Einzig and colleagues* elsewhere in this issue of MINNESOTA MEDICINE has attempted to define a normal course for decay of serum CPK activity after cardiac surgery. Deviation from this course, the authors suggest, will assist in the identification of myocardial infarction. They define a logarithmic curve of enzyme activity decay with respect to time. The curve has a narrow standard deviation, although the return of activity to normal levels varied between day three and day eight after surgery. The problem is complicated, as the authors note, by the fact that most serum CPK activity after cardiac surgery is probably non-cardiac in origin. One is looking for deviations in a small fraction of activity, against a large non-specific background.

Recent post-operative studies of CPK isozymes[1] suggest an alternative approach to the diagnosis of myocardial infarction by identification of a myocardium-specific CPK fraction in the serum. preferably combined with LDH isozyme studies. Increase of the activity of this fraction in the serum during the post-operative course implies myocardial infarction. This approach appears promising.

Frederick Muschenheim, M.D.
Minneapolis, Minnesota

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*See page 683.

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Long Fiberoptic Colonoscopy

Long fiberoptic colonoscopy is an exciting new modality. This instrument has opened new vistas in this field of medicine and is the answer to a lifelong dream of many who have previously been frustrated by their inability to accurately evaluate lesions above the reach of the sigmoidoscope. Most pedunculated lesions and certain sessile polypoid lesions in any part of the colon can now be removed with a snare through this instrument. Indeed the operation of colotomy and polypectomy seems destined to be relegated to surgical history. The differential diagnosis of inflammatory bowel disease has been aided in no small measure by colonoscopy.

Granted that the advantages and benefits of colonoscopy are great, it must be appreciated that the procedure is not a simple one and that major hazards may be encountered. Perforations of the colon have occurred in the hands of some examiners. Hemorrhages which could be life-threatening have also been reported as has a laceration of the spleen. These complications have been reported by experienced examiners as well as by beginners in the use of the instrument. Concerning polypectomy through the colonoscope Dr. Christopher Williams,[1] endoscopist at St. Mark's Hospital in London, has said: "However, to obtain a full view of a polyp and to snare and retrieve it often requires the utmost in technical skill and an inexperienced endoscopist employing diathermy techniques may not only endanger the patient but also achieve poor results."

Fiberoptic colonoscopy is not a procedure which should be performed as part of a routine physical workup. It should not be put into the same category as proctosigmoidoscopy. Since the examination does require the services of a physician, one or more assistants, and is costly and time consuming it should be undertaken only when certain criteria have been met. For the present the following guidelines seem appropriate: (1) Fiberoptic colonoscopy should be performed only when the barium enema x-ray examination fails to yield adequate information or reveals a lesion which requires additional information which direct vision can furnish. (2) The examination should never be performed unless adequate bowel preparation has been achieved. An attempt to pass the colonoscope in a bowel inadequately prepared is worthless, a waste of time and effort. (3) Active, major hemorrhage should be considered a contraindication as should active, acute inflammatory bowel disease especially in the presence of peritoneal irritation.

To become an expert at performing fiberoptic colonoscopy one should be in a setting where frequent examinations are performed. This is not a procedure which should be attempted by the occasional examiner. Dr. Hiromi Shinya,[2] one of the leading experts in this field, has stated that he did not feel comfortable using the scope until he had performed two hundred examinations. Not only can the passage of the scope be extremely difficult but the interpretation of what the examiner sees requires much experience. One trained in proctosigmoidoscopy is not ipso facto an expert in evaluating lesions as seen thru the colonoscope.

We have in long fiberoptic colonoscopy a procedure which has great potential for good. Let us not abuse the opportunity which is ours by prostituting the procedure and risking the possibility of tarnishing its reputation. A word to the wise should be sufficient!

William C. Bernstein, M.D.
St. Paul, Minnesota

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*Emeritus Clinical Professor of Colon and Rectal Surgery, University of Minnesota Medical School, Minneapolis.

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1. Williams, Christopher: Colonoscopy Gut 14:990, 1973.
2. Shinya, Hiromi: Personal Communication.

Dermatology—October Issue

The next issue of Minnesota Medicine will be devoted to the problems in dermatology commonly seen by nondermatologists.

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X-ray Conference

Spine Changes in a 20-Year-Old Black Male

The patient, a 20-year-old black grain harvester, is admitted for chronic, low-back pain and multiple self limited attacks of abdominal pain. On physical examination he has scleral icterus, a grade II systolic ejection murmur, and a tender abdomen. Laboratory examination reveals a hemoglobin of 8.9 gm./100ml, W.B.C. 14,200 with 80% pmn's, reticulocyte count of 15%, and total bilirubin of 3.6 mg./100ml.

A spine film was obtained (Figure 1). What is your diagnosis? (See next page).

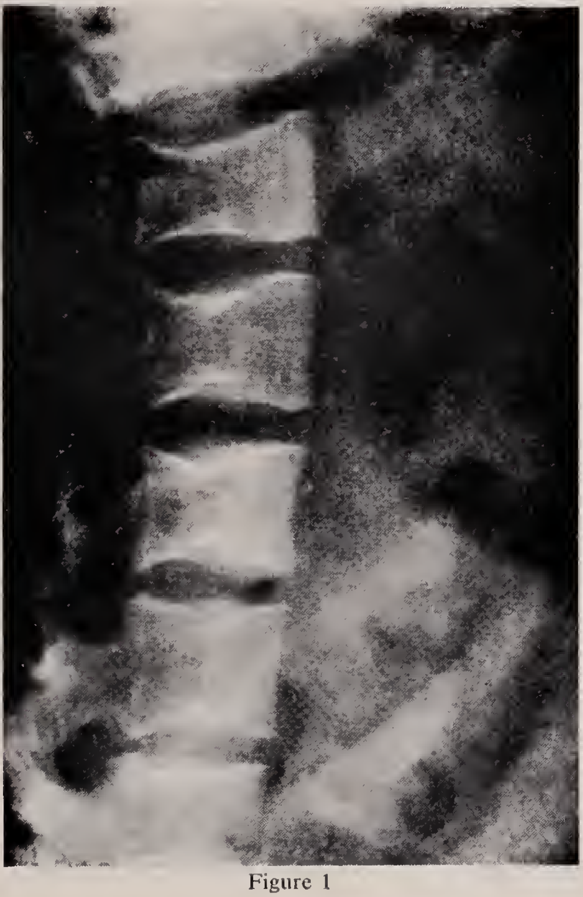

Figure 1

Diagnosis: Sickle Cell Disease

The lateral spine film demonstrates the "fish vertebra" seen in sickle cell disease and codfish. The central portion of the vertebral bodies are depressed with a normal margin at the periphery The cancellous bone shows coarse, thickened trabeculae. Similar appearing vertebral bodies can be seen in osteoporosis or multiple myeloma, but unlike sickle cell disease, have a smooth, continuous, depressed end plate. Figure 2 illustrates this difference. Some authors consider multiple "fish vertebra" to be a specific sign of sickle cell disease. However, a case of thalassemia major has been reported showing the identical vertebral deformity.[1] The deformed spine does not always cause clinical symptoms.

Two theories attempt to explain the vertebral deformity of sickle cell disease. According to Henkins, cancellous bone of the vertebral body is weakened by loss

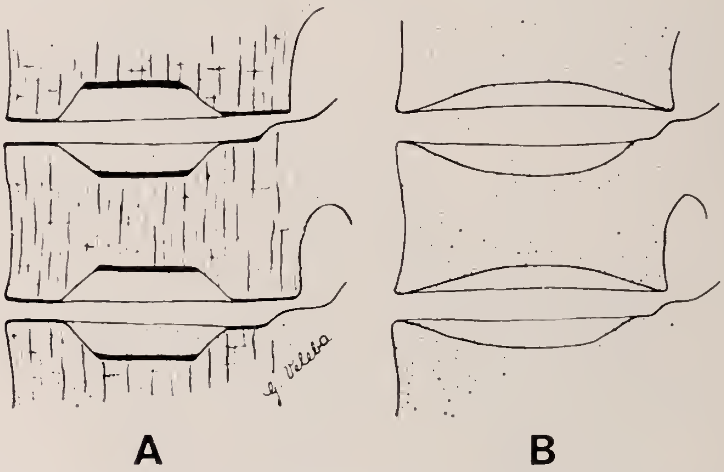

Fig. 2—Drawing of abnormal vertebral centra in lateral projection: (A) Distinctive contour seen in sickle cell disease. (B) The non-specific, biconcave shape produced by the compression of weakened bone which may be seen in a number of skeletal disorders. (Illustration from Reynolds J: The Roentgenological Features of Sickle Cell Disease and Related Hemoglobinopathies. Springfield, Illinois, Charles C. Thomas Publisher, 1965.)

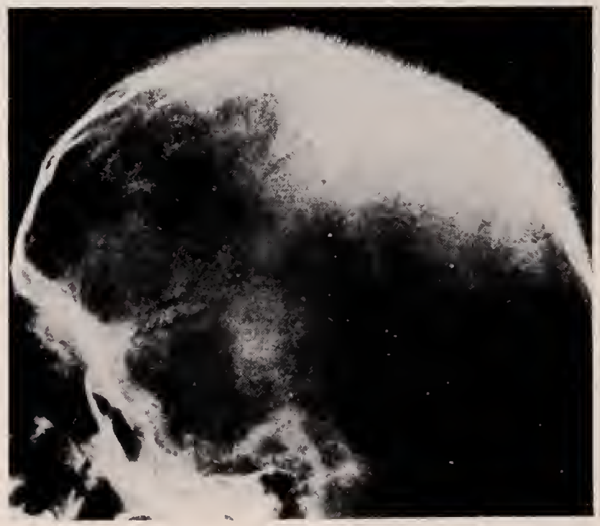

Fig. 3—"Hair on end" appearance of the skull caused by radial striations of persistent diploic trabeculae is seen more commonly in hereditary spherocytosis and thalassemia major.

of trabeculae caused by repeated episodes of ischemic necrosis. Pressure from the nucleous pulposus then deforms the weakened body.[2] More recently, Cockshott states that local ischemia to the cartilaginous end plate retards vertical growth of the centrum.[3]

Other skeletal changes seen during the course of sickle cell disease include: generalized osteoporosis, osteosclerosis, infarcts of long bones, avascular necrosis of the femoral or humoral heads, and osteomyelitis. The "hair on end" appearance of the skull seen uncommonly is shown in Figure 3.

Two primary pathologic processes cause the bone abnormalities. Firstly, marrow red cell hyperplasia, secondary to the chronic anemia, causes a generalized deossification and decrease of the supporting trabeculae. The remaining trabeculae thus appear coarse and irregular. Secondly, the sickled cells can occlude the nutrient arteries of bone causing bone infarcts with secondary osteosclerosis.[4]

Sickle cell disease also causes changes in the internal organs that can be seen radiographically. The most common finding is non-specific cardiomegaly seen in over 90% of adults with sickle cell disease. Gallstones occur more commonly, presumably related to the increased bilirubin breakdown from hemolyzed red cells. Ten percent of children with sickle cell disease have an enlarged spleen which occasionally calcifies. Adults usually have a shrunken, fibrotic spleen secondary to repeated infarcts. Renal papillary necrosis can rarely be seen on IVP.[5] Finally, priapism, caused by venous stasis of sickled cells, is a most distressing complication occurring in 3-5% of male sicklers.[6]

Ted Berman
Phase D medical student
University of Minnesota

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Request for Physician's Art Work

For many years the Board of Editors of MINNESOTA MEDICINE has recognized and supported photographic and other artistic talents of the members of the Minnesota State Medical Association publishing cover pictures in color of their work. Our series of color covers have received much favorable comment and many journals have followed us in the use of color art in this manner.

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Farrell Stiegler, M.D.
Cover Editor

Chemical Dependency

Is Pessimism about Alcoholics Justified?

JON R. WEINBERG, PH.D.*

Pessimistic attitudes about alcoholics are primarily a function of experiences based on: (1) idealized conceptions of improvement, plus the problem of the clinical error, (2) failure to intervene until the late stages, (3) inappropriate intervention for the prognosis, and (4) unintentional enabling of the pathological drinking behavior. Physicians can play a key role in modifying all these variables. Our culture as a whole is moving at a rapid rate towards both awareness of alcohol problems and their eminent treatability. Among all professions, medicine has the greatest opportunity to advance the trend toward early recognition and appropriate intervention. Many physicians already have discovered how gratifying it is to see the dramatic improvements in their properly treated alcoholic patients. The day may be close at hand when an air of justified optimism will prevail among physicians in general as a function of their helpful behavior.

THE ANSWER TO THE title question is "it depends". Many physicians tend to feel pessimistic about the prognosis for alcoholics, and their belief is often reinforced by experience. Others, especially those who work directly in the field of alcoholism rehabilitation, are likely to feel comparatively optimistic and their belief is also reinforced by experience. It may be helpful to specify some of the variables which may be significant in making an accurate individual prognosis, and in generating a favorable outcome.

Definition of Improvement

Alcoholism is a chronic relapsing condition. Some doctors consider any drinking by a recovering alcoholic as evidence of failure. It would be more helpful to think in terms of overall improvement in functioning. To cite an extreme example, an individual who drinks to the point of impaired functioning on 100 days of the year would be considered to be a failure, but this may represent a substantial improvement over a previous rate of 250 days per year impairment. This is little different from an obesity case who often departs briefly from the diet but still chalks up a substantial weight loss over time. Although the goal of lifetime sobriety is an ideal which some do indeed achieve, most alcoholics will have some relapses. This is hardly surprising considering both the nature of the illness and our cultural milieu which fosters alcohol use. It is critical that the physician not react with condemning judgments or a tone of hopelessness when a relapse occurs. This would simply add to the individual's low self-esteem and guilt. The focus should be on what changes might be made to decrease the probability of future relapses.

A related issue is what may be called the clinical error. This is the normal tendency of practitioners to generalize from the patients seen in their offices or in hospitals. Since many of the medical problems of alcoholics are secondary to their drinking, patients who keep returning for care are those who most often are not improving. Patients whose improvement is substantial will naturally reduce or eliminate regular physician visits. While alcoholism treatment facilities do careful follow-up of all their patients and learn about the many "invisible" cases of improvement, individual medical practitioners rarely seek such information and tend to forget former patients. This clinical error may have a potent influence on the pessimism variable, as one is most frequently seeing the least successful cases.

Stage of Intervention

It is well known that the more advanced the stage of alcoholism, the poorer the prognosis for successful intervention. This is partially related to the strengthening of the denial system.[1] The primary implication for the physician is to attempt to implement effective intervention strategies as early as possible in the progression of the illness. Physicians have often avoided direct confrontation with earlier stage alcoholics, probably due both to the social stigma attached to the problem and lack of training in early detection. Physician referrals for specialized treatment have often been based on serious medical complications, which usually reflect 15 years or more of a manifest alcohol problem. Such referrals will unquestionably tend to foster reinforcement of pessimistic attitudes as a result of a relatively low rate of successful outcomes. Diagnostic screening using sophisticated interviewing techniques,[2] followed by appropriate treatment prior to the late stage, may be expected to generate substantial improvement in the majority of patients.

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*Director of Training and Education, Hennepin County Alcohol and Drug Program; Clinical Asssitant Professor of Psychiatry and Psychology, University of Minnesota; and Private Practice. Address reprint requests: 6490 Excelsior Boulevard, St. Louis Park, Minnesota.

Level of Intervention

Prior to discussing levels of alcoholism intervention, a critical distinction must be made: *Detoxification is not treatment for alcoholism, only for intoxication.* Physicians are advised to clarify this distinction for patients, lest they consider themselves to have been in treatment for alcoholism when they were simply detoxified. Similarly, physicians should not modify their prognostic expectation when a patient simply undergoes "drying out" for a few days in a hospital, as the basic problem—the illness of alcoholism—has in no way been affected. Detoxification is, of course, an appropriate preparation for alcoholism treatment.

For convenience, three levels of treatment intervention are distinguished, labeled minimal, moderate, and maximal. The minimal level involves discussions by the physician or other professional with both patient and spouse regarding the nature of the drinking problem and formulation of a careful plan for modification of alcohol use, generally involving abstinence. This minimal level may be appropriate when the prognosis appears excellent. The key variables in such a prognosis are: (1) relatively brief history of the problem, ordinarily less than five years, (2) the patient fully accepts the problem and is strongly committed to solve it, and (3) environmental supports in the form of family, friends, and job factors appear generally positive, that is, a cessation of drinking will be reinforced rather than sabotaged.

A moderate level of intervention involves a referral to a non-residential resource specializing in alcoholism problems. In the vast majority of cases, this means Alcoholics Anonymous, a world-wide self-help group program known to everyone. Twin City physicians are generally surprised to learn that there are over 300 AA groups in their metropolitan area. In some geographic areas, other specialized alcoholism resources may be available, such as outpatient clinics or private institutes. Anywhere in Minnesota, a call to the nearest Alcoholism Information and Referral Center will provide assistance. Referral to a mental health practitioner or agency is not recommended unless there has been demonstration of special competence with the alcoholic population. This moderate level of intervention is suggested when the prognosis is good. This means: (1) the patient demonstrates a fair degree of insight and motivation, (2) environmental supports are available and primarily positive, so that no unusual stresses are likely, and (3) the planned intervention has not been previously tried unsuccessfully. The moderate level may be implemented out of necessity for patients when the maximal level is more appropriate but simply cannot be arranged, e.g., the patient and family refuse residential treatment.

The maximal level of intervention is residential treatment at a specialized alcoholism facility, typically involving a stay of one month or more. Numerous such facilities, both public and private, are available throughout Minnesota. Considering the global impact this illness has on the life of its victims and their families, and the extensive changes involved in successful recovery, it is important for physicians to accept that a high proportion of patients well into the middle stage or beyond will require residential treatment. Furthermore, many of these will need to be recycled through treatment one or more times in order to benefit. Patients who do not meet the criteria for the two other intervention levels should be assumed to be suitable for the maximal level. The primary exception to this would be patients whose prognosis is too poor to recommend any available treatment. This means cases of substantial cerebral impairment, severe social deterioration with advanced age, or those who have been cycled through treatment many times with no benefit. Such people are usually more suitable for humane custodial care.

The most typical error by professionals is to recommend a lesser level of intervention than the prognosis justifies, resulting in poor outcomes and a feeling of pessimism. Of course, recommending the appropriate level is not necessarily followed by the patient agreeing to it. In these cases, the patient should at least be asked to make a commitment, with the mate present, to follow the suggested plan should his way fail. Anytime the result at the minimal or moderate levels proves unsatisfactory, the next intervention should advance a level. If the patient repeatedly refuses to cooperate with a necessary maximal intervention, the physician's best strategy, in many cases, is to counsel the family to consider arranging a more coercive element, such as a petition for an inebriety commitment or perhaps a legal separation, to increase the probability of helpful action. Many alcoholics have entered residential treatment purely because a court has ordered it, or solely to get a spouse back, and left treatment with a strong personal commitment to sobriety. In other words, internal motivation is neither essential nor even expected prior to residential treatment.

Enabling versus Confrontation

The critical issue of how the individual's social environment often fosters and maintains the destructive drinking pattern was partially discussed in the author's earlier article on denial.[1] If the physician is to find reinforcement for hopeful rather than pessimistic attitudes, he must address himself as to how he can impact the environment to foster constructive intervention. The two most likely avenues of impact available to the physician are the family and the doctor-patient relationship itself. A third possibility, the employer, would be an especially excellent avenue whenever the physician happens to be in a position to arrange such involvement.

With regard to the family, the physician is advised to make a careful assessment as to whether their actions are enabling the alcoholic to continue his drinking behavior. It is particularly common for wives and mothers to cover up for the alcoholic in the sincere belief it is helpful and loving to do so. The professional must attempt to persuade the family that the only loving thing to do is to allow the suffering to occur, even though this may entail social embarrassment, financial deprivation, or inconvenience to other family members. Allowing the alcoholic to suffer is often perceived as a paradox, because in our culture illnesses ordinarily call for a response of relieving suffering. The family must be led to understand that, because of the profound dependence on the chemical, there is no reason to expect positive change unless the results of drinking become more painful than the prospect of sobriety. Unless this key issue is successfully resolved, the prognosis will be dim. This principle is also of obvious importance if the question of commitment or separation is raised as these acts are not usually considered loving.

Since some alcoholics have no relatives whose help can be profitably solicited, it is sometimes incumbent on the physician to try to impact the patient without additional assistance. This means, first and foremost, elimination of the enabling role. Never ignore the drinking problem. Every contact with the patient, at least by a primary-care physician, should include some discussion of the problem, even if only briefly, whether or not the appointment is for an alcoholic-related complaint. This is comparable to discussing the heavy smoking of an emphysema victim whose current office visits is for his bursitis. Do not hospitalize someone under a sole diagnosis of gastritis or pancreatitis or other such disorder when alcoholism is primary. (Recent legislation in Minnesota requiring all group health insurance policies to reimburse for alcoholism treatment will help avert that obstacle to proper diagnosis.) In short, never pretend the problem doesn't exist, even though the patient would love it if you did.

A second point relates to the content of the discussions in which the physician attempts to confront the patient with his problem. Because of their traditional emphasis on physical health, most medical professionals place primary stress on how alcohol use is damaging the body. In some cases this includes frightening predictions of imminent death or disability. Such approaches are not only ineffective but may prove harmful. While objective facts about physical ramifications must be stated to the patient as a matter of information, the intentional induction of fear will rarely serve as more than a very temporary incentive, and might even drive the patient to submerge the fear in yet another bout with the chemical. A more helpful approach is to deal with other aspects of the patient's life which alcohol use is impairing. In what ways is his behavior harmful to other people? Is he functioning the way he would like to in his relationships with others, in his work, in his internal psychological comfort? Flippant denial of such problems initially need not discourage the physician from tactful but persistent probing beyond the facade of bravado.

Many physicians may feel they lack the time and skill to engage in the discussions described. In some cases, the patient may then be persuaded to accept a referral, not for treatment, but for consultation about his alcohol use. When this occurs, the physician should be prepared to arrange an immediate contact with the suggested resource and then stay informed about the patient's involvement. Again, one may call the nearest Alcoholism Information and Referral Center, as well as any other agencies or individuals the physician may find helpful in his own community.

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Takayasu's Syndrome

This syndrome consists of chronic obstruction of the great vessels branching from the aortic arch, which results in syncopal attacks, ocular symptoms, absence of pulses in the neck and arms, and evidence of collateral arterial circulation. This vascular disturbance was first described by Takayasu, a Japanese ophthalmologist, in 1908. Subsequently 57 cases have been reported in the Japanese literature. Less than 40 additional cases have been reported in the world literature, mainly by European writers. Since the excellent descriptions by Martorell and Fabre in 1944 and in 1954, the condition has also been referred to as "Martorell's syndrome." It has been observed most frequently in young women and seldom occurs in persons over 40 years of age.

Clinically the condition is characterized by diminished or absent pulsations in the carotid, axillary, brachial, and radial arteries. No great vessels are evident on angiograms. It is not possible to record the blood pressure of the upper extremities, although hypertension of the lower extremities is usually marked. Rib notching is often present, associated with prominent collateral arterial circulation frequently manifested as a bruit. Symptoms of circulatory ischemia may include claudication, syncopal attacks, hypersensitivity of the carotid sinus reflex, hemiparesis, and convulsions. Numerous changes may be observed in the fundus oculi, including atrophy of the iris, retinal pigmentation and atrophy, cataracts, and corneal opacities. The eye symptoms usually appear by the age of 25 years; hence, the occasionally applied term "young female arteritis." Other less frequently involved lesions of the head and neck area are nasal septum perforation, trophic skin changes of the face, and claudication of the jaw muscles.

The cause of this syndrome is not known. Many patients have had a preceding rheumatic-like infection. Atheromatous plugging of arteries, allergic-hyperergic factors, and thrombosis secondary to the arteritis are etiologic considerations. Histologically the vascular lesions show evidence of inflammatory reaction with cellular infiltration and the presence of giant cells.

The condition is progressive, and the prognosis is poor. Death usually occurs after a few years, although survival for 20 years after onset of symptoms has been reported. Prophylactic anticoagulant therapy is indicated. Davis and associates* have successfully treated one case surgically.

Durham, Robert H.—Encyclopedia of Medical Syndromes
Hoeber Medical Division, Harper and Row, New York

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Change in Health Care Services

For Indian Americans

JOSEPH WESTERMEYER, M.D., M.P.H., PH.D.*; RICHARD TANNER†
AND JEAN SMELKER, M.D.‡

The director of a community clinic recognized the urgent health needs of urban Indian people. In order to improve services for Indian people, two steps were taken. First, all available job slots were filled by non-certificated Indian people. Second, an Indian supervisor was given responsibility for all non-certificated employees. New Indian staff members undertook activities within existing programs. No specific programmatic changes were made, nor were new programs undertaken. Neither the composition of the neighborhood board nor their advisory role in the clinic changed. There were no consumer movements involved at the clinic. The clinic director remained at her job. Non-Indian patients continued to attend the clinic as before. Care was *not* rendered along ethnic lines, but rather along functional task-oriented lines. Major changes in health care for Indian patients resulted. Scheduled appointments, number of new registrants, and emergency care all rose spectacularly. Child protection cases fell precipitously.

COMMUNITY CLINICS have been designed to bring modern health care facilities to the underprivileged. Such clinics have encountered a variety of problems, among them being rapid staff change over and under-utilization by the target population. Case studies indicate that traditional methods for solving such problems in a clinical setting have often not functioned well.[1,2]

Behavioral scientists and administrative experts have suggested means to remedy these problems in the health care system. Suggestions have included the greater involvement of the community in designing and implementing programs, endowment of power in an indigenous board of directors, hiring neighborhood health aides, learning the language of the community.[3-11] Unfortunately, most of these changes have not been implemented along with health care evaluation so that we might examine whether they produce any demonstrable change in health care services.

Method

This paper presents a case study in which the planned change was to hire neighborhood people from the target population (Indian Americans) to work as receptionists, secretaries, lab assistants, health care aides, and neighborhood health aides. An Indian supervisor was also assigned to be responsible for the ten new non-certificated (i.e. non-professional) workers at the clinic. The members of the advisory board were not changed, nor was the advisory nature of the board. No new programs were begun during the period under evaluation. None of the non-Indian staff learned to speak Chippewa or Sioux. Nor was the service organized so that Indian staff worked only with Indian patients. An Indian patient might receive his entire care during a given visit from non-Indian staff members (who still comprised the majority of workers at the clinic). Conversely, non-Indian patients might be assisted wholly by Indian staff.

Background

The Community-University Health Care Clinic (CUHCC), established in 1967, serves the health needs of children and adolescents in a Minneapolis "core city" neighborhood. Many elderly White people live in the area. The adolescents and children in the area are a composite of White, Black, and Indian people.

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Young Indian people have the highest mortality rates of any demographic group in Minnesota. Neonatal deaths have been decreasing in the rural reservation areas (where the Indian Health Service has been active), but remains quite high in Minneapolis. Infants and young children of Indian heritage have a high death rate from infectious disease, while adolescents have a high death rate from violence. Indian children are placed in foster homes, federal boarding schools, and state guardianship at an alarming rate.[12,13]

In the face of these urgent health needs among the Indian young, CUHCC soon directed major efforts toward the Indian sub-population. Not only did their efforts meet with only limited success, but the traditional *modus operandi* of the predominantly white, highly-trained staff led to crisis situations which actually alienated the Indian community. Some of these incidents have been reported previously.[14]

The Data

Scheduled Appointments

During January, February and March of 1971, prior to the hiring of Indian staff, ninety-six (96) Indian children had scheduled appointments at the clinic. In the same three months of 1972, three hundred and eleven (311) Indian children had scheduled appointments at CUHCC.

Thus, the number of Indian children being seen at scheduled appointments (i.e. non-emergent or non-episodic visits) more than tripled during the trial period (indeed, after only six months into the trial period). This increase was not accounted for by the increase of Indian registrants alone, since the number of new Indian registrants had not yet begun to increase at that time.

New Indian Registrants

During April, May and June of 1971, prior to the hiring of Indian staff, there were twenty-four (24) new Indian registrants; they comprised 24% of all registrants at that time. During the same three months of 1972 (i.e. several months into the trial period), there were forty-four (44) new Indian registrants; they comprised 49% of all registrants.

Thus, in both relative numbers and absolute numbers, the new Indian registrants about doubled in this time period from 1971 to 1972.

Emergency and Crisis Care

There was concern that an emphasis on health maintenance and on scheduled appointments might have acted to reduce care for unregistered Indian children and adolescents, especially those with acute health problems. Therefore, unregistered Indian children receiving care for three acute infectious disorders (upper respiratory infection, strep throat, and otitis media) were tabulated.

During the first six months of 1971, prior to the hiring of Indian staff, twenty-eight (28) unregistered Indian children received care for these acute infectious disorders. During the same six months of 1972, fifty-two (52) unregistered Indian children received care for these disorders. Of equal interest, the number of acute otitis media cases actually decreased slightly during this time (from eleven down to nine cases), while the number of URI and strep cases increased 2.5 times (from seventeen up to forty-three).

These data indicate that the clinic was providing more emergency care to Indian children than in the past. Moreover, they suggest that chronic middle ear disease—a common health problem among local Indian people—may have been ameliorated by better access to emergency services.

Child Protection Cases

In the two years prior to the grant, eight cases at the clinic were reported to the Child Protection Unit of the Hennepin County Welfare (involving both Indian and White children). In the year since the trial was operative and the Indian workers hired, no cases have been reported to this Unit by CUHCC.

This change was not due simply to disappearance of child neglect. Rather it was due to a change in emphasis on keeping the family together by helping both the parents and the children. Where one out-of-family placement of an Indian child was indicated, an Indian family was found for the placement; and the child's family collaborated in the placement without any legal constraints being exerted upon them.

Discussion

With few exceptions, majority institutions and their programs have failed to benefit Indian people.[15] In view of these past failures, the achievements at the urban clinic described in this paper were extraordinary ones. After a relatively short period of time, improvements could be demonstrated.

Also remarkable was the simplicity of the innovations. These consisted of: (1) the hiring of ten Indian workers from the neighborhood (some with no training) and (2) the assignment of one Indian worker to a supervisory capacity (responsible for all non-certificated employees). Beyond these administrative changes ordered by the clinic director, the Indian staff developed their own approaches within the formats and programs already under way at the clinic.

The Indian staff chose educational approaches that have been effective in other clinical settings. Personal interaction and group discussion were emphasized, methods endorsed by Carlow[16] and Lindaman.[17] The often popular "T-group" or "sensitivity" approach, a method shown by Benedict et al. to produce no significant change in an institutional setting,[18] was not used. Also notable by their absence were complex, often disruptive, and usually expensive change maneuvers, such as human relations training, scholarly consultation, third party intervention, community power movements, or laboratory training.[4,19,20]

The sudden presence of Indian staff members (comprising one-third of the staff at the end of the year) did not impede care to non-Indian children and adolescents. They continued to seek care at the clinic as before. New registrations by non-Indians actually increased somewhat during the year when Indian staff first joined the clinic, and then plateaued at its former level.

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*The next day, at five in the morning, d'Artagnan got up, went downstairs himself to the kitchen, asked (among other ingredients, of which the list has not come down to us) for wine, oil, and rosemary, and, his mother's recipe in his hand, made himself a balm which he applied to his numerous wounds, changed his bandages himself, and would not admit the addition of any other physician. Thanks no doubt to the efficacy of the Bohemian balm, and perhaps also thanks to the absence of any doctor, d'Artagnan was on his feet that very evening.**

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*Alexandre Dumas: The Three Musketeers. Chapter 1. 1844.

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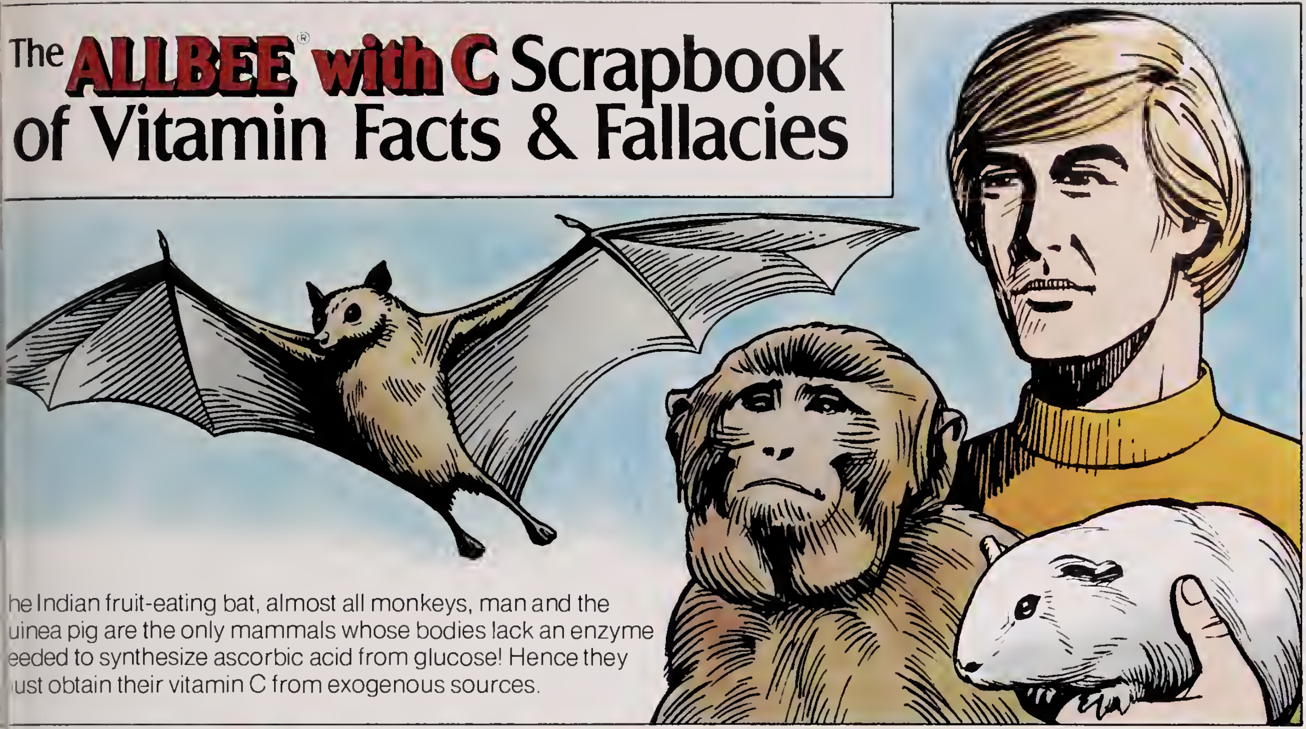

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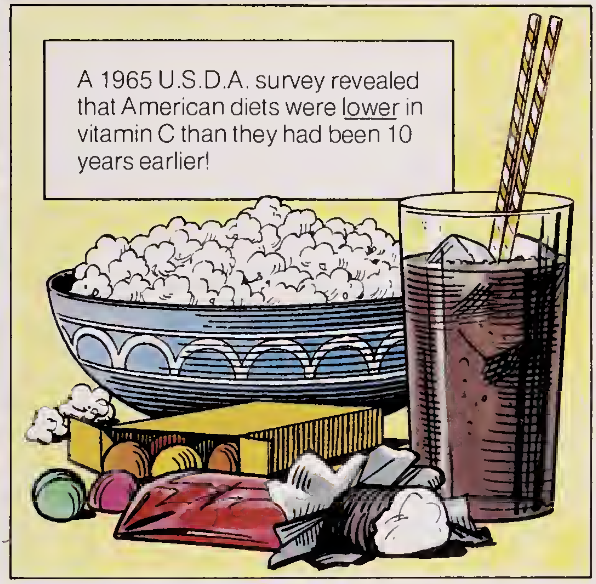

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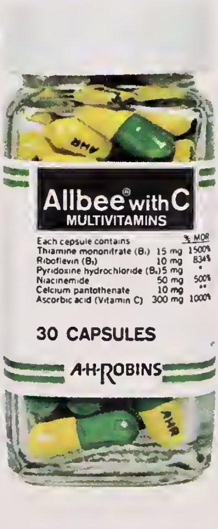
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Fracture Conference

Arthrograms of the Ankle

Their Role in Acute Trauma

EINER W. JOHNSON, JR., M.D.* AND JOHN W. BEABOUT, M.D.†

Dr. Einer W. Johnson, Jr.:

As an introduction to arthrography of the ankle, I would like to tell you about a 21-year-old man who came to our emergency room about 9:00 one night. He had been hurt while trimming a tree. A large limb had fallen on his left knee while the knee was flexed at 90°, and his foot was trapped in the crotch of the tree. He had immediate pain in his left ankle. On admission, the ankle was very swollen. An Xray was taken (Figure 1).

Dr. William C. MacCarty III:

I can't see any fracture in the region of the calcaneus or the talus.

Dr. Johnson:

Why are you looking for a fracture in that particular region?

Dr. MacCarty:

The accident probably caused a compression force on the ankle, and the two ankle bones that would be decompressed are the calcaneus and the talus.

Dr. Johnson:

I think that is good reasoning. Here is a patient with his knee flexed to 90° and his foot locked in the crotch of a tree when a heavy limb strikes the superior aspect of his knee. In effect, the knee-ankle dimension is shortened. There was a flake fracture off the side of the talus. The ankle was put in a Robert Jones dressing. When we removed the Robert Jones dressing four or five days later, the ankle was still very swollen and very tender on both the lateral and medial sides, but it was particularly tender along the medial side under the medial malleolus. Thus, the injury probably involved more than just a flake fracture off one side of the talus.

Dr. MacCarty:

I guess his knee was all right from what you have said.

Dr. Johnson:

There was no trouble in his knee.

Dr. MacCarty:

You might have taken some stress films to determine whether he had a ligamentous injury to that ankle. I don't know if tomograms would help in getting reliable Xrays of the talus or calcaneus.

Dr. Johnson:

What impressed me was the tenderness under the medial malleolus.

Dr. MacCarty:

He must have had a compression fracture of either the talus or calcaneus, but I don't see it.

Dr. Johnson:

Could he have had anything else? If you don't break a bone, what else can happen?

Dr. MacCarty:

Stress a ligament somehow.

Dr. Johnson:

Stress films weren't taken when he first came to the emergency room, and when we finally saw him three to four days later, he had so much pain and distress that we couldn't take stress films.

Dr. MacCarty:

Even if you put him to sleep?

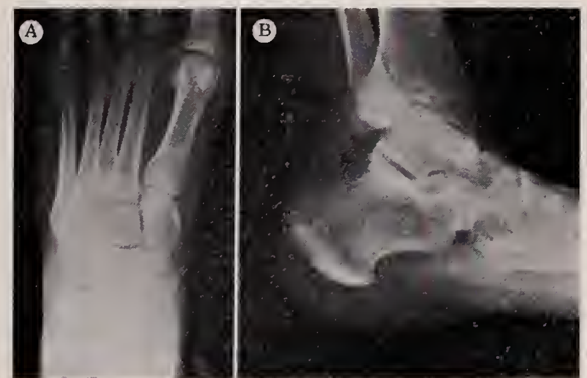

Fig. 1—Left ankle. *(A)* Anteroposterior view. *(B)* Lateral view.

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†Consultant, Department of Diagnostic Roentgenology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Fracture Conference, April 2, 1973.

Dr. Johnson:

We thought about that, but we wondered about the wisdom of injecting contrast medium into the ankle to take some stress films.

Dr. Richard T. Dauphine:

I think that he might have had some ligamentous injury on the medial side—a deltoid ligament rupture. I would put the patient under general anesthesia, take the stress films, and plan to repair whatever damage was done.

Dr. Richard A. Fink:

I think that arthrography could be done.

Dr. Johnson:

Is there some question about the reliability of arthrograms?

Dr. Fink:

I think there is. But I think that a gross tear might show up well on an arthrogram.

Dr. Johnson:

That is exactly what we did (Figure 2). Here is a man with a severe ankle injury but not much bony change. Is this an abnormal arthrogram?

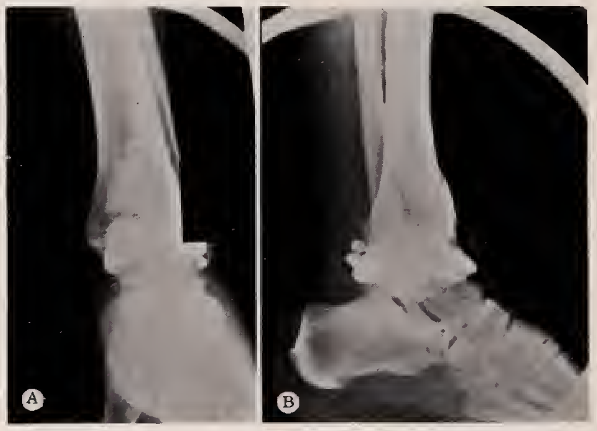


Fig. 2—Left ankle. *(A)* and *(B)* Anteroposterior and lateral views showing contrast medium located within ankle joint and ascending into region of torn interosseous ligament.

Dr. Fink:

Yes.

Dr. Johnson:

We did arthrography because we thought that some ligaments were torn.

Dr. Fink:

The deltoid looks good.

Dr. Johnson:

Do you think that is important?

Dr. Fink:

Yes.

Dr. Johnson:

The condition of the deltoid is probably the most important finding on this arthrogram. If this man has rupture of the deltoid ligament, he is in serious trouble. What is the diagnosis?

Dr. Fink:

I think he has a tear of his interosseous membrane.

Dr. Johnson:

And from what you have seen, do you think there is anything else?

Dr. Fink:

I can't see anything, but mechanically there should be something else wrong.

Dr. Johnson:

Again I say that what disturbed me about this young man was seeing him several days later with so much tenderness under the medial malleolus. Of all the injuries about the ankle, deltoid ligament rupture is one of the more severe and, if unrecognized, will produce a worn-out ankle joint very quickly. So it is important to recognize the deltoid tear. I am not sure whether overlooking a lateral ligamentous tear is critical, although this is a point of argument. But if you miss a deltoid tear, you have overlooked a situation or a chain of events that will produce a degenerated joint. To me the important thing in doing arthrography in this instance is to determine whether or not this man, with tenderness on the medial side of his ankle, has a deltoid ligament rupture. And if this exists surgical repair is indicated.

Dr. Richard S. Bryan:

I would like to present an opposite viewpoint. I don't think such a patient should be operated on. I think there will be a good response if the cast is kept in place long enough. I think the mistake in conservative treatment is not leaving the cast on long enough.

Dr. Patrick J. Kelly:

What are you going to do with the patient who has a torn ligament caught between the medial malleolus and talus?

Dr. Bryan:

I think such tears are rare, at least according to the literature. Tears on the lateral side, however, occur more frequently. Cases in which the lateral ligaments are caught within the joint and have to be removed are common.

Dr. Richard N. Stauffer:

Because of the location of the attachment of the deltoid ligament, trapping the deltoid within the ankle mortise is extremely unlikely, and conservative treatment is probably adequate.

Dr. Hubert A. Tressler:

The first Xrays (Figure 1) show some compression of the lateral aspect of the tibia, so-called lateral plate compression. I am wondering if that isn't the patient's worst injury.

Dr. Johnson:

We have made the diagnosis of a diastasis, and generally you can't have an isolated diastasis without having some other change. To recognize the diastasis was probably the most important thing, but we were concerned in the beginning about the deltoid ligament. Probably the worst ankle injury is a fracture of the distal fibula, with a deltoid ligament rupture and widening of the ankle mortise. This widening is blamed on the fractured fibula, and the deltoid ligament injury is unrecognized. This case can serve as a good introduction to the subject of arthrography of the ankle.

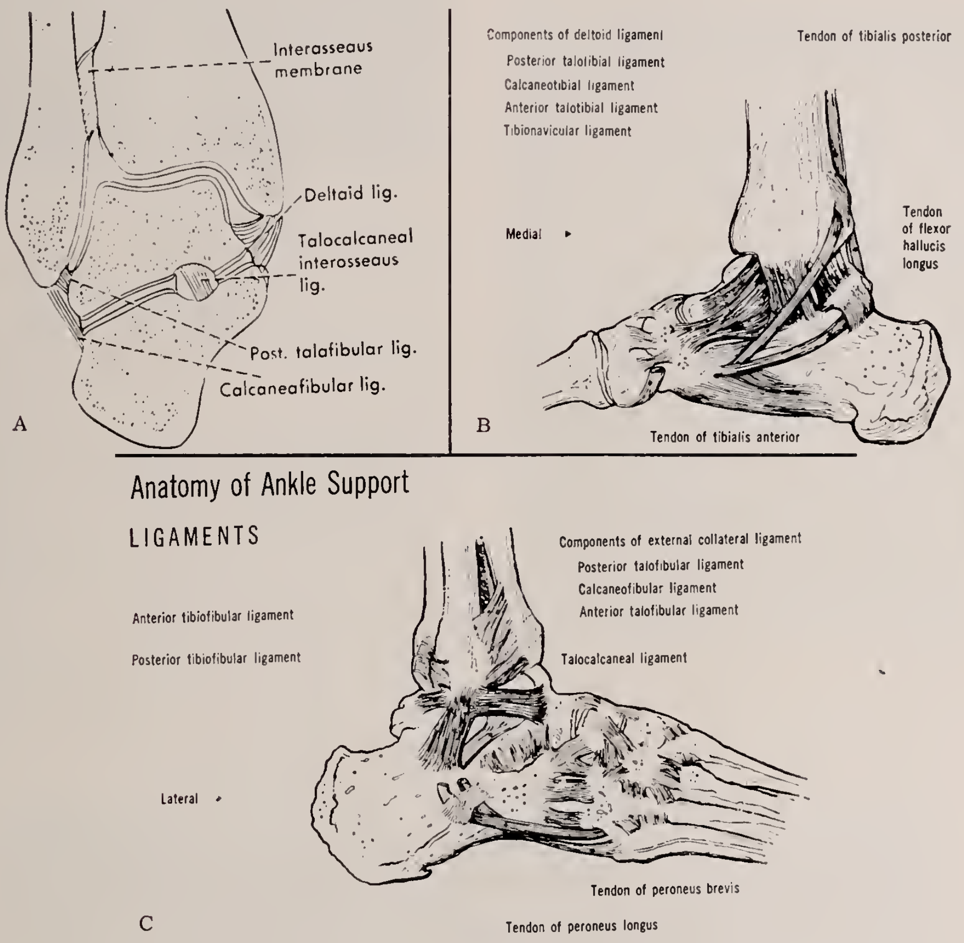
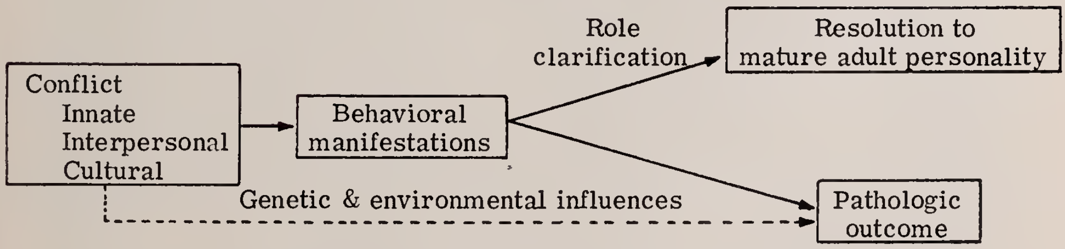

Interasseaus membrane
Deltaid lig.
Talocalcaneal interosseaus lig.
Post. talafibular lig.
Calcaneofibular lig.
A
Components of deltoid ligament
Posterior talotibial ligament
Calcaneotibial ligament
Anterior talotibial ligament
Tibionavicular ligament
Tendon of tibialis posterior
Medial
Tendon of flexor hallucis longus
Tendon of tibialis anterior
B
Anatomy of Ankle Support
LIGAMENTS
Anterior tibiofibular ligament
Posterior tibiofibular ligament
Components of external collateral ligament
Posterior talofibular ligament
Calcaneofibular ligament
Anterior talofibular ligament
Talocalcaneal ligament
Lateral
Tendon of peroneus brevis
Tendon of peroneus longus
C

Fig. 3—Anatomy of ankle support. *(A)* Posterior view. (From Hollinshead WH: Anatomy for Surgeons: The Back and Limbs. Vol 3. New York, Hoeber Medical Division, Harper & Row, Publishers, 1958. By permission.) *(B)* Medial view. *(C)* Lateral view. (B and C from Spring JM, and Hyatt GW: Treatment of sprained ankle. GP 36:78-94, 1967. By permission of the American Academy of Family Physicians.)


Conflict
Innate
Interpersonal
Cultural
Behavioral manifestations
Role clarification
Resolution to mature adult personality
Pathologic outcome
Genetic & environmental influences

The ankle is a compound joint. The close union of the tibia and the fibula is necessary to produce an ankle joint. The posterior view (Figure 3A) of the ankle shows the cavity that ascends superiorly off the ankle joint into the interosseous membrane. In arthrography, a certain amount of contrast medium normally goes into this space. The deltoid ligament can be seen in the medial view (Figure 3B). The deltoid is not one structure but a series of structures with deep and superficial layers. A lateral view (Figure 3C) shows three definite ligaments that can be torn from front to back. When a lateral ligament of the ankle joint is torn, the anterior talofibular ligament tears first. With more severe sprain or with continuation of the strain, the calcaneofibular ligament ruptures, and finally the posterior talofibular ligament ruptures.

In arthrography, we use an image intensifier. The main reason for this is that if some contrast medium gets outside the ankle joint you can determine if it escaped from a hole in the synovium. We thought that it was better to give our patient a local anesthetic and perform arthrography rather than use general anesthesia and take stress films.

Tubing (Figure 4) is used so that you can fluoroscope the ankle while injecting contrast medium into the joint without having your hands in the x-ray field. It is a good practice to use the image intensifier to follow the course of the contrast medium as it is injected into the joint. The average ankle joint takes only three to five ml of medium. Thus, when we could put 10 ml of contrast medium into the joint, we had some indication of the diagnosis. Because we could inject contrast medium into the joint as fast as we could press the plunger of the syringe, there had to be a rupture of the synovium of the ankle joint.

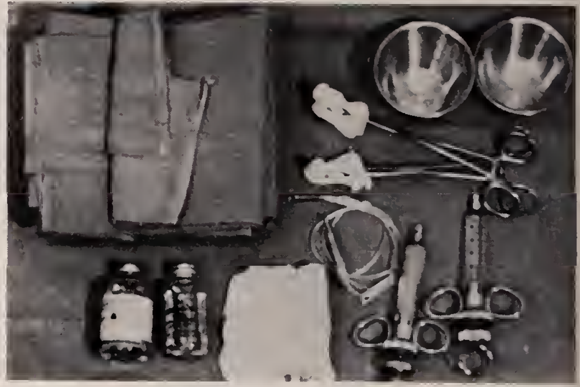


Fig. 4—Material for arthrography.

The synovium is attached at the margin of the cartilage of the ankle joint, and if the ligaments tear, they are in close approximation to the synovium. Thus, the synovium tears as well. So, if you have a rupture in the synovium, you undoubtedly also have a rupture of one of the ligaments. If you are in the emergency room and you want to determine whether or not there is a tear of the synovium, which would indicate a ruptured ligament, you could put saline or lidocaine into the joint. If you could inject 10 ml of saline or lidocaine into the joint quickly, you know that a ligament has been ruptured.

After the contrast medium is injected, we take anteroposterior, lateral, and right and left oblique views of the ankle. Dr. Beabout is going to discuss the normal and abnormal arthrograms.

Dr. John W. Beabout:

In filming, a mistake that can be made is

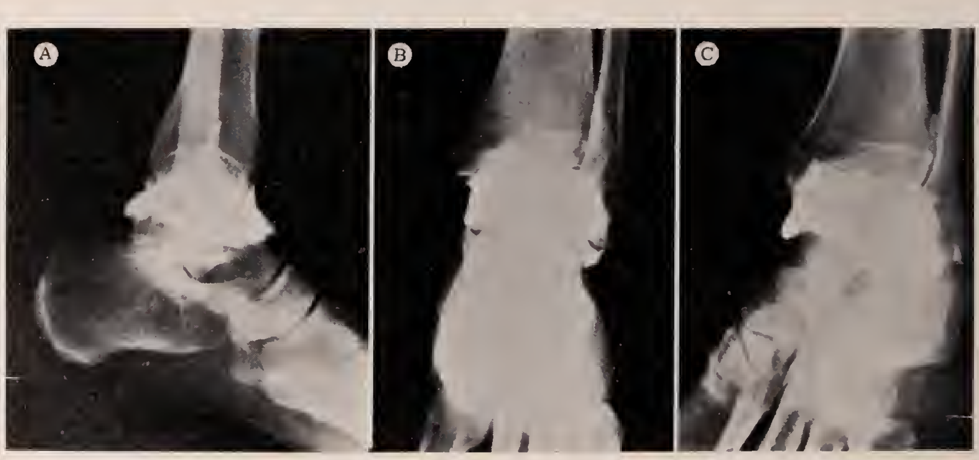


Fig. 5—Normal arthrogram of ankle. *(A)* Lateral view showing normal recesses anteriorly, posteriorly, and superiorly. *(B)* Anteroposterior view. *(C)* Oblique view demonstrating superior recess.

taking spot films. These films are of poor quality. Films taken by an overhead x-ray tube are much better, even if you have to move the patient to another table. Basically, what we are looking for is a tear in the joint capsule, and such a tear is identified by extravasation of contrast medium outside the capsule. This is secondary evidence of an associated ligament tear since the ligaments are closely associated with the capsule. By localizing the area of extravasation, you can indirectly identify the ligaments that have been torn. So, first we need to know what the normal ankle joint looks like.

A normal lateral view (Figure 5A) shows two recesses, one anteriorly and one posteriorly. The recesses contain loose folds of synovium that allow the foot to take the plantar position and to dorsiflex. And there is also a small recess superiorly that goes between the tibia and fibula. The anteroposterior view (Figure 5B) shows a small amount of contrast medium gathering into the recess between the tibia and fibula. The medium may extend superiorly for 2.5 cm in the normal ankle. On the lateral aspect of the joint you see a small bulge inferiorly, but none of the contrast medium dissects around the lateral malleolus, and medially there is no bulging at all. The oblique view (Figure 5C) shows the recess between the tibia and fibula. This is probably the best view for visualization of a lateral capsule tear, because it shows the lateral malleolus in profile.

There are several variations of normal that are important. Some contrast medium goes into the posterior aspect of the talocalcaneal joint in Figure 6. In about 15% of normal ankles a communication exists between the ankle joint and the posterior talocalcaneal joint. There is another normal variant, seen in about 20% of the population, in which contrast medium enters a tendon sheath inferior to the joint (Figure 6). The tendon sheath can be easily localized by obtaining an anteroposterior film. If the tendon sheath is in a medial location, as it was in our case, it is either the flexor hallucis longus or flexor digitorium lon-

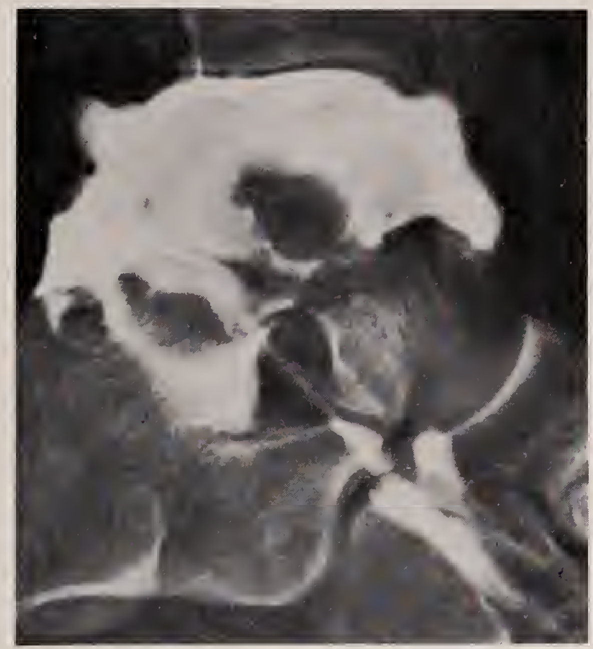


Fig. 6—Normal variations. Lateral view shows communication of ankle joint with posterior talocalcaneal joint. There is communication with flexor hallucis longus tendon sheath inferiorly. Its medial position is determined on anteroposterior view.

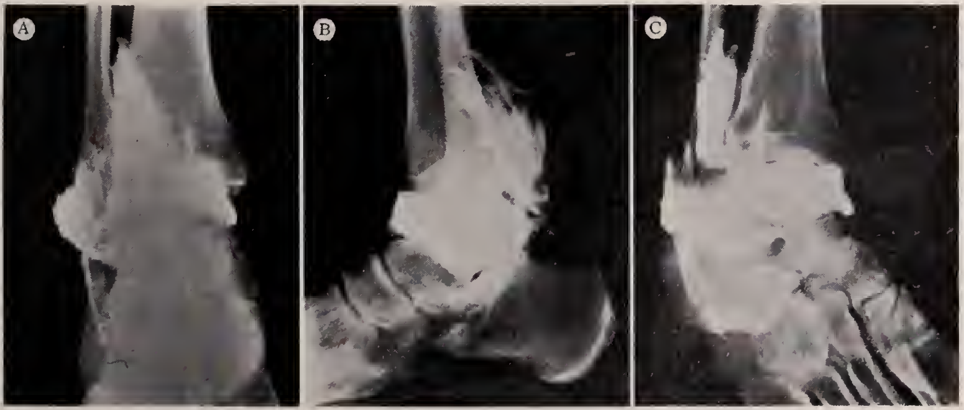


Fig. 7—Abnormal ankle arthrogram demonstrates tear of anterior talofibular, calcaneofibular, and inferior tibiofibular ligaments. Anteroposterior *(A)*, lateral *(B)*, and oblique *(C)* views show filling of laterally located tendon sheath, indicating tear of calcaneofibular ligament. In *(A)* and *(C)* tip of lateral malleolus is obscured by contrast medium, diagnostic of anterior talofibular ligament tear. *(A) (B)* and *(C)* show rupture of superior recess secondary to tear of inferior tibiofibular ligaments.

gus and is a normal variant. However, there is never any filling of a laterally placed tendon sheath in the normal ankle.

In a deltoid ligament injury, contrast medium is extravasated into the soft tissues of the medial malleolus. On the lateral aspect of the ankle there are three ligaments that can be ruptured, starting anteriorly with the anterior talofibular ligament. On the anteroposterior film, contrast medium extravasates into the soft tissues lateral to the malleolus and extends superiorly over the fibula (Figure 7A). This is diagnostic of an anterior talofibular ligament tear. With a tear of the calcaneofibular ligament, there is usually communication with the tendon sheath of the peroneus tendons, and this will be seen inferiorly. You can see the filling defect of the tendon within the sheath. This demonstrates the importance of knowing whether the tendon sheath that filled is located medially or laterally. The third injury that we can see here is the diastasis between the tibia and fibula, with the tear of the inferior tibiofibular ligaments. The lateral view (Figure 7B) shows contrast medium in the tendon sheaths inferiorly and the extravasation superiorly between the tibia and fibula. The oblique view (Figure 7C) shows the diastasis between the tibia and fibula and the contrast medium covering the lateral malleolus. Contrast medium in the peroneus tendon sheath is also shown.

In ankle arthrography, it is important that proper films be taken promptly. The contrast medium should remain about 20 to 30 minutes—long enough to get the necessary views.

So, we'll go no more a-roving
So late into the night,
Though the heart be still as loving,
And the moon be still as bright.

For the sword outwears its sheath,
And the soul wears out the breast,
And the heart must pause to breathe.
And love itself have rest.

Though the night was made for loving,
And the day returns too soon,
Yet we'll go no more a-roving
By the light of the moon.*

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*Byron, "So We'll Go No More A-Roving"

Laboratory Letter

Anemia Pointer: Check The MCV

The academic boys have been whooping it up about the Mean Corpuscular Volume (MCV). At least that's what we gathered from two recent Yale articles.[1,2] In both papers the authors rally round the MCV as measured on the Coulter Counter-S as a rapid, inexpensive, and automated way to screen, classify, and pursue anemias. They have a good point.

So if you detect a low hemoglobin in your office, perhaps you should consider following it with a Coulter CBS. That way, in one short swoop, you can confirm the hemoglobin and also look at the MCV.

MCV

Why the MCV? Because you can use it to classify anemias as normocytic (80 to 100 cubic microns) microcytic (79 cubic microns or less), or macrocytic (101 cubic microns or more).

Just to give you a feel for the relative numbers of these types of anemias, we recently went over 1057 consecutive Coulter CBC's submitted to our laboratory. We used as a criterion for anemia a hemoglobin below 14.0 Grams/100 ml in men and a hemoglobin below 12.0 Grams/100 ml in women.

TABLE 1
Percent of Anemic Patients Found Among CBC's done on Coulter Counter Model S

	Normal Hemoglobin	Low Hemoglobin	Percent of Anemias
Men	300	63	17%
Women	540	144	21%
	840	207	20%

Comments

Twenty percent, of course, is a high incidence of anemia for normal people. No doubt this high rate results from physicians referring anemic patients to our laboratory. A better idea of the rate of anemia among the populace can be gained from the Permanente Group's work in California. There investigators recorded anemia in 1.9 percent of men and 12.6 percent of women among 44,653 outpatients undergoing multiphasic examinations.[3] The Permanente figures match closely those of Hervey,[4] who observed that 12.6 percent of 73,783 female blood donors had a hemoglobin of less than 12.3 grams/100 ml.[4]

Why is anemia so common in women? Partly because of increased iron requirements due to menstruation and pregnancy (Table 2). A woman loses about 50 ml of blood in each period and requires about 680 more mg of iron in pregnancy than in nonpregnancy.

TABLE 2
Iron Requirement of Women and Others

Patient	Daily Iron Requirement
Normal Men and non-menstruating women	5-10 mg/day
Menstruating Women	7-20 mg/day
Pregnant Women	20-48 mg/day
Adolescents	10-20 mg/day
Children	4-10 mg/day
Infants	1.5 mg/kg

Relative Numbers

Although the figures are skewed towards anemia, they still provide a useful opportunity to examine the relative numbers of normocytic, microcytic, and macrocytic anemias (Table 3).

TABLE 3

Percent of Types of Anemia as Classified by the MCV on the Coulter Counter Model S

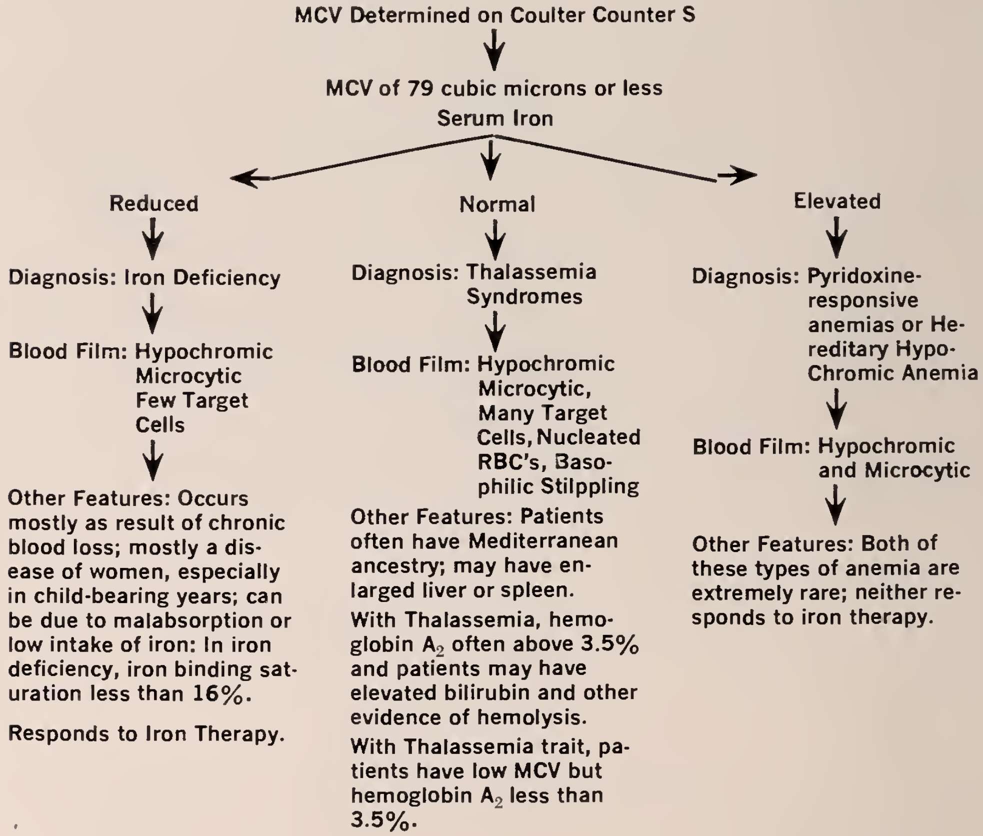
Number of Anemic Patients	Normocytic	Microcytic	Macrocytic
Men, 63 patients	45	15	3
Women, 144 patients	107	18	6
	152	33	9
Percent of Total Anemias	79%	16%	5%

Normocytic Anemias

If your patient's anemia is normocytic, as almost 80 percent are, you have narrowed down the possibilities some. At least you've effectively excluded macrocytic anemias, such as pernicious anemia, and microcytic anemias, as in significant iron deficiency. As far as the normocytic anemias themselves go; they accompany many chronic diseases, and are also present with sudden blood loss, hemolytic processes, malignancies, renal disease, liver disorders, bone marrow failure, blood dyscrasias, and hemoglobinappthies.

Microcytic Anemias

If your patient's anemia is microcytic, you have a good chance of skewering the cause. As indicated below, only a limited number of possibilities exist.



MCV Determined on Coulter Counter S

MCV of 79 cubic microns or less

Serum Iron

Reduced

Diagnosis: Iron Deficiency

Blood Film: Hypochromic Microcytic Few Target Cells

Other Features: Occurs mostly as result of chronic blood loss; mostly a disease of women, especially in child-bearing years; can be due to malabsorption or low intake of iron: In iron deficiency, iron binding saturation less than 16%.

Responds to Iron Therapy.

Normal

Diagnosis: Thalassemia Syndromes

Blood Film: Hypochromic Microcytic, Many Target Cells, Nucleated RBC's, Basophilic Stilppling

Other Features: Patients often have Mediterranean ancestry; may have enlarged liver or spleen.

With Thalassemia, hemoglobin A_2 often above 3.5% and patients may have elevated bilirubin and other evidence of hemolysis.

With Thalassemia trait, patients have low MCV but hemoglobin A_2 less than 3.5%.

Elevated

Diagnosis: Pyridoxine-responsive anemias or Hereditary Hypo-Chromic Anemia

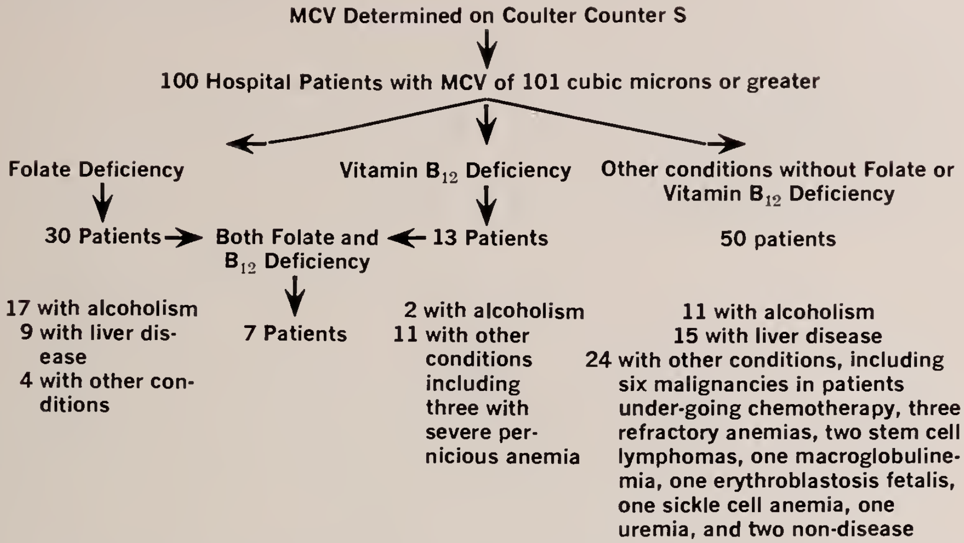
Blood Film: Hypochromic and Microcytic

Other Features: Both of these types of anemia are extremely rare; neither responds to iron therapy.

Macrocytic Anemias

In many physician's minds, macrocytic anemia is virtually synonymous with pernicious anemia. Small wonder. The picture of a large-eared, blue-eyed, lemon-skinned patient, often of Scandinavian origin, was drilled into us in medical school. So the association of pernicious anemia with macrocytic anemia is easy to make. As in many diseases, the spectrum of causes of macrocytosis has changed.

At Yale-New Haven Hospital, anyway, investigators checked serum folate and serum B_{12} levels on 100 patients with macrocytosis and reported this spectrum of causes of macrocytosis.[1]


MCV Determined on Coulter Counter S
100 Hospital Patients with MCV of 101 cubic microns or greater
Folate Deficiency
Vitamin B12 Deficiency
Other conditions without Folate or Vitamin B12 Deficiency
30 Patients
Both Folate and B12 Deficiency
13 Patients
50 patients
7 Patients

17 with alcoholism
9 with liver disease
4 with other conditions

2 with alcoholism
11 with other conditions including three with severe pernicious anemia

11 with alcoholism
15 with liver disease
24 with other conditions, including six malignancies in patients under-going chemotherapy, three refractory anemias, two stem cell lymphomas, one macroglobulinemia, one erythroblastosis fetalis, one sickle cell anemia, one uremia, and two non-disease

Because the Yale study showed an unexpectedly dominant role of alcoholism, we performed 100 consecutive Coulter CBS's on known alcoholics admitted to the Hazelden Foundation in Center City, Minnesota with these results:

TABLE 4
Incidence of Macrocytosis and Anemia among 100 Alcoholics Admitted to Hazelden for Detoxification

Number of Patients		Number of Patients with Anemia	Mean Value for MCV	Macrocytosis With Anemia	Macrocytosis Without Anemia
Men,	67	Two (both normocytic)	98	0	15
Women,	33	Two (both macrocytic)	100	2	15
Total	100	Four	99	2	30

Role of Alcoholism

In their way, perhaps our little studies of 1057 consecutive outpatient CBC's and of 100 CBC's on known alcoholics reveals why alcoholism cropped up so often as a cause of macrocytosis (30 of 100 hospital patients) in the Yale study. After all, if only five percent of 1057 outpatients had a macrocytic anemia (another one percent had macrocytosis with anemia), yet the rate among alcoholics ran 30 percent, doesn't that mean the alcoholics ran five times the rate as the outpatients? Perhaps. But perhaps not, too. Statistics are tricky things. In any event, alcoholics run a higher rate of macrocytosis.

Comment About Macrocytosis

What can be learned from information? Well, in the first place, alcoholism or liver disease constitutes the most common cause of red cell macrocytosis (54 percent is the Yale Study). Secondly, these alcoholism and liver diseases usually produce a folic acid deficiency—although a B_{12} deficiency can occur. Thirdly, malignancy, especially in patients undergoing chemotherapy with antimetobolites and inhibitors of nucleic acid synthesis, is an important and growing cause of macrocytosis. And, fourthly, straightforward pernicious anemia makes up only about 10 percent of the current causes of macrocytic anemia.

Summary

The Mean Courpuscular Volume (MCV), as measured electronically on the Coulter Counter Model S, is a rapid, inexpensive, and automated way to classify anemias. We found 79 percent of anemias are normocytic, 16 percent are microcytic, and 5 percent are macrocytic. The best followup test for microcytic anemia is a serum iron; and the recommended followup tests for a macrocytic anemia are the serum folate and serum B_{12}. Iron deficiency from blood loss in women is the most common cause of microcytic anemias; and alcoholism (with or without liver disease) is the most frequent reason for macrocytosis (with and without anemia).

Richard L. Reece, M.D.
Minneapolis, Minnesota

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3. Collen MF et al.: Dollar cost per positive test for automated multiphasic screening. New Eng J Med, 283:459-463, 1970.
4. Hervey GW et al.: Low hemoglobin levels in women as revealed by blood donor records. JAMA 149: 1127, 1952.
5. Hattersley PG: Macrocytosis of the erythrocytes. JAMA, 189:997, 1964.
6. Editorial: Diagnostic tests for iron deficiency. Ann Intern Med 75:640, 1971.
7. Committee on Iron Deficiency. JAMA, 203:407, 1969.

Community Referral Sources

A number of sources are available to physicians seeking information on community service organizations for referral purposes. The following is one such source:

180 Degrees Re-Entry Center
236 Clifton Avenue
Minneapolis, Mn. 55403
335-2772; 335-1608 Office; 332-9592 Residence

Services	*Days/Hours*	*Eligibility*	*Fees*
Re-entry center for chemically dependent males and females who are ex-felons	24 hours/day	Must be ex-felon, adult	Often paid by welfare or client
Individual Counseling	When needed		
Group counseling through scheduled group meetings			
Therapeutic experience program			

Community services directories are available from the Community Health and Welfare Planning Councils in Minneapolis and St. Paul. For a directory of metropolitan youth-serving agencies. The Catalogue can be obtained from Enablers, Inc., 1238 Baker Building, 706 Second Avenue So., Minneapolis, Minnesota 55402.

Clinical Path Conference

Conditions Complicating Myocardial Infarction

Clinical-Pathologic Correlation in 60 Cases

ZEEV VLODAVER, M.D.[*]; DANIEL E. HILL, M.D.[*]; JAMES N. KARNEGIS, M.D.;[*]
AND JESSE E. EDWARDS, M.D.[*]

In a previous study, two of the authors (DEH, JNK) reported the clinical spectrum observed in 451 patients who had been admitted to the coronary care unit of the Miller Division of United Hospitals and in whom the clinical diagnosis of acute myocardial infarction was established according to criteria described.[1] In that series there were 99 fatal cases representing a mortality of 21.8 per cent. Autopsy was done in 60 of the 99 fatal cases.

The purpose of this study was to determine the pathologic findings in the 60 autopsied cases in order to correlate the clinical and pathologic findings of acute myocardial infarction.

The time of confinement in the coronary care unit varied. In most instances, this occupied four to five days following which the patient was transferred to the general area of the hospital. In each case of this study, the patient had not left the hospital following admission to the special unit. Seven of the patients were hospitalized for periods of time varying from 15 to 50 days.

As used here, the term acute myocardial infarction represents a condition in which there is pathologic evidence of acute ischemic necrosis of the myocardium. Since this process may not be dentifiable pathologically for some time after ts onset (12-18 hours), it is recognized that certain cases of acute myocardial infarction might be eliminated from this designation on the basis of lack of pathologic confirmation. In other instances, lack of pathologic confirmation may, in fact, mean that no acute myocardial necrosis had been present, in spite of the clinical picture of acute myocardial ischemic disease. Using the above criteria for acceptance of acute myocardial nfarction as an entity, 12 of the 60 autopsied cases were eliminated from this analysis of acute myocardial infarction. The analysis that follows will concern itself principally with the 48 cases in which acute myocardial infarction was confirmed pathologically. The 12 cases in which this diagnosis was not confirmed will be reviewed briefly after the primary analysis.

Definition of Terms

The conditions leading to death from acute myocardial infarction were classified either as pump failure or electrical failure. Pump failure was said to be present when there were signs of acute pulmonary edema or shock occurring either alone or together. Cases of pump failure could be further subdivided according to whether or not rupture of the heart was demonstrated at autopsy. This led to identification of four subgroups of pump failure as follows.

1. *Left ventricular failure.* This designation was characterized clinically by severe dyspnea with pulmonary rales. Pathologically, pulmonary edema was present and rupture of the heart absent.

2. *Shock.* Shock was manifested by pallor, sweating and brachial systolic blood pressure levels less than 100 mm. Hg. Pathologically, pulmonary edema was not significant and rupture of the heart was not present.

3. *Left ventricular failure and shock.* When the two foregoing coexisted, this designation was employed.

4. *Rupture of heart.* Clinically, this might resemble the categories of left ventricular failure and/or shock or electrical failure. Pathologically, rupture of a ventricular structure was demonstrated, among these being the free wall of the left ventricle, the ventricular septum or a papillary muscle.

The term electrical failure was applied when

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a sudden collapse of the circulation resulted from a dysrhythmia and occurred in the absence of rupture of the heart. The collapse of the circulation was usually associated with a demonstrable major ventricular arrhythmia.

Observations

Acute Myocardial Infarction

Sex and Age

Of the 48 subjects with autopsy confirmation of acute myocardial infarction, there were 20 male and 28 female subjects. Of the ten patients who were below 60 years of age, six were male and four, female. In subjects over the age of 60 years, there was a higher number of female subjects (24 females to 14 males).

Acute Myocardial Infarction: Clinical Manifestations in the 48 Autopsied Cases (Table 1)

Among the 48 autopsied cases, 35 had manifested pump failure and 13, electrical failure. The most common type of pump failure, as defined above, was left ventricular failure, being seen in 17 cases. Shock alone or left ventricular failure and shock without rupture occurred in four cases each.

Rupture of heart accounted for ten of the 35 with pump failure. Nine of the ten cases of rupture occurred in women.

TABLE 1

Clinical Manifestations in 48 Cases of Acute Myocardial Infarction Studied at Necropsy.

Pump failure	35
Left ventricular failure	17
Shock	4
Left ventricular failure and shock	4
Rupture of heart	10
Electrical Failure	13

Association of Healed Infarction and Clinical Patterns

Among the 48 cases with acute myocardial infarction, scars of healed infarction (Figure 1) were observed in 31 (64.5 per cent) of the cases. In nine of the 13 cases (68 per cent) manifesting electrical failure, healed myocardial infarction was associated, while in 22 of the 35 cases (63 per cent) with pump failure such an association was present. If one eliminates from the group with pump failure those with rupture of the heart, in which scars were uncommon, there were 21 of 25 in which healed myocardial infarction was associated (84 per cent).

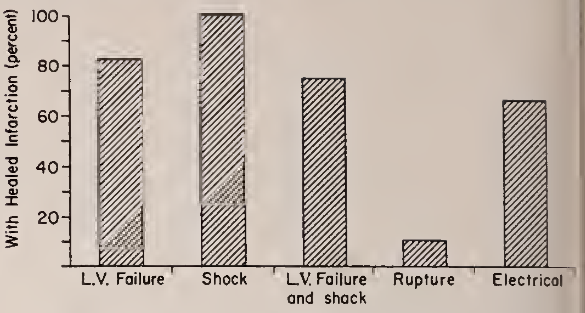

Fig. 1—Incidence of healed myocardial infarction in association with acute myocardial infarction according to the clinical manifestations in 48 autopsied cases.

Location of Acute Infarction and Relationship to the Clinical States (Table 2)

Of the 22 cases in which the acute infarct was located in the anterior wall, 19 manifested pump failure, while in three of these electrical failure was the immediate cause of death. In 11 cases the infarct was located in the inferior wall; eight were complicated by pump failure and three by electrical failure. Of the 15 cases with infarction either of the lateral wall alone or the anterior and inferior walls together, pump failure or electrical failure were equally distributed.

TABLE 2

Clinical Manifestations Related to Site of Acute Myocardial Infarction.

Location	Total No.	Pump Failure	Electrical Failure
Anterior wall	22	19	3
Inferior	11	8	3
Lateral wall	5	3	2
Anterior and inferior	10	5	5
Total	48	35	13

Type of Infarction and Relationship to Complications (Table 3)

In the 35 cases with pump failure, the acute myocardial infarction was transmural in 26 cases (75 per cent), while in the remaining nine cases of pump failure, the acute infarction was subendocardial. A different picture was obtained in the group of 13 cases with "electrical failure." In five of these (39 per cent) transmural infarction was present while in eight (61 per cent) the acute infarction was subendocardial.

TABLE 3

Relationship of Type of Acute Myocardial Infarction to Pump Failure and to Electrical Failure in 48 Autopsied Cases of Acute Myocardial Infarction.

Type of acute infarction	Pump Failure (35 cases)	Electrical Failure (13 cases)
Transmural	26 (75%)	5 (39%)
Subendocardial	9 (25%)	8 (61%)

In the 17 cases with left ventricular failure.

nine showed transmural and eight subendocardial infarction. Among the eight cases with shock with or without left ventricular failure, in seven the infarction was transmural in nature. Each of the cases with rupture of the heart exhibited transmural infarction.

Type of Infarction and Relationship to Sex of Patients

Acute transmural myocardial infarction was more common among female patients and acute subendocardial was more common in the male (Table 4).

TABLE 4

Types of Acute Myocardial Infarction According to Sex of Patients.

	Male	Female
Acute transmural infarction (31 cases)	10 (32%)	21 (68%)
Acute subendocardial infarction (17 cases)	10 (59%)	7 (41%)

Among the 31 patients with acute transmural myocardial infarction, ten were male and 21 were female, representing 32 per cent and 68 per cent, respectively. Among the 17 cases with subendocardial infarction, ten were male and seven were female, representing 59 per cent and 41 per cent.

When acute myocardial infarction was associated with healed infarction there was no significant sex difference (17 males; 14 females) (Table 5). On the other hand, when no healed infarction was associated, females were more commonly represented than males by a ratio of 12 to five. This factor may explain, in part, the higher incidence of rupture of the heart among female subjects. The latter condition classically is not associated with myocardial scars.

TABLE 5

Association of Healed with Acute Myocardial Infarction according to Sex of Patients.

	Male	Female
Acute infarction alone (17 cases)	5 (29%)	12 (71%)
Acute and healed infarction (31 cases)	17 (55%)	14 (45%)

Acute Coronary Thrombosis in Acute Myocardial Infarction

Acute coronary thrombus was present in 27 of 48 cases (56 per cent) of acute myocardial infarction.

Among the 31 cases with acute transmural infarction, 21 showed acute coronary thrombosis (68 per cent), while in the group of 17 cases with acute subendocardial infarction, recent coronary thrombus was present in six (35 per cent).

In those patients that survived one or two days following the onset of acute transmural infarction, recent coronary thrombosis was present in half of the cases. In those who survived three days or more after the onset of infarction, the incidence of recent thrombosis rose, being present in over two-thirds of these patients (Figure 2).

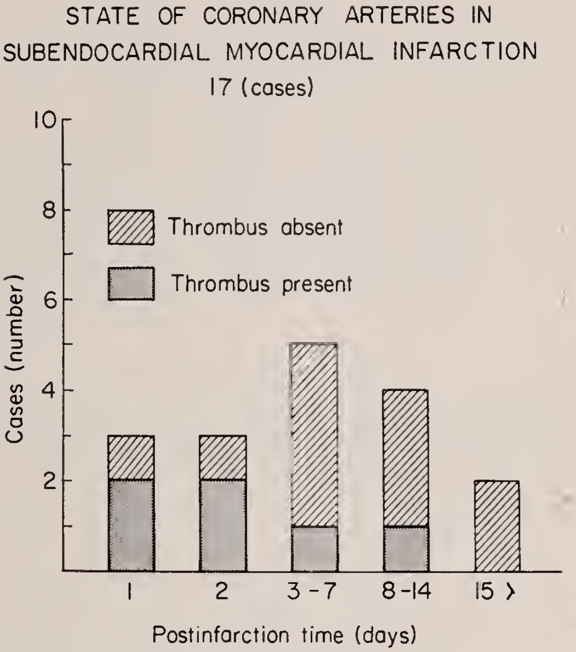

Fig. 2—Incidence of acute coronary occlusion in 31 patients with acute transmural myocardial infarction according to the postinfarction time.

The tendency for an increased incidence of coronary thrombosis with time after the onset of transmural infarction was not demonstrated among the subjects with subendocardial infarction (Figure 3).

Acute Myocardial Infarction Absent

In 12 of the 60 cases in which autopsy had been done, acute myocardial infarction was not demonstrated in spite of the fact that this had been the clinical diagnosis.

Two were examples of acute dissecting aneurysm of the aorta. Two other patients died within hours of admission to the coronary care unit. Six of the patients were examples of unstable angina and showed moderately elevated serum levels of myocardial enzymes. In each case the electrocardiogram had shown marked ST depression as evidence of acute subendocardial myocardial ischemia. The time of death varied from

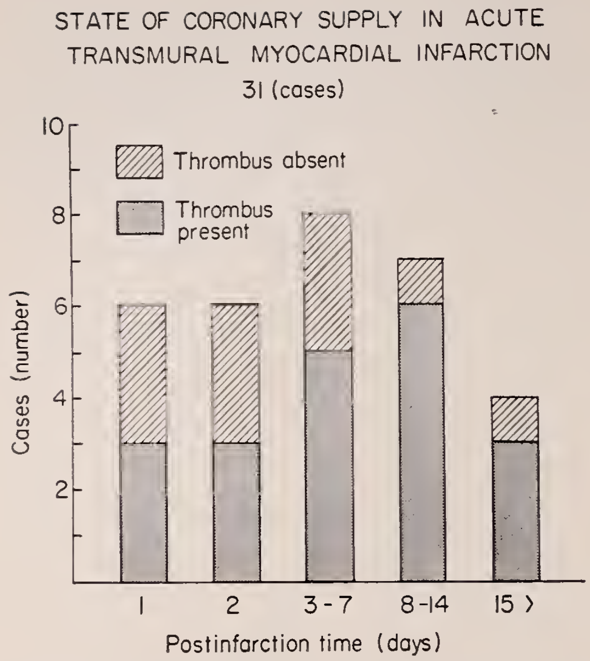

Fig. 3—Incidence of acute coronary occlusion in 17 cases of acute subendocardial myocardial infarction according to postinfarction time.

six to 24 days after admission.

In the remaining two cases, death occurred 37 and 40 days, respectively, after admission with classical clinical evidence for acute myocardial infarction. Death in each was electrical in type. In these cases, the scar tissue observed may have, in part, resulted from acute infarction present on admission.

Comment

This clinico-pathologic study on acute myocardial infarction serves to emphasize certain features of this disease among subjects who fail to survive acute myocardial infarction.

The inordinately high incidence of female to male subjects among fatalities as compared to admissions may relate to the higher incidence of transmural infarction in the female as compared to the male. This, in turn, may relate to the fact that the coronary care unit is more effective in managing disturbances of rhythm than pump failure. Pump failure is more commonly associated with transmural than subendocardial infarction and is consistent with the greater amount of loss of muscle in transmural infarction than in subendocardial.

A contribution to pump failure of acute infarction particularly in the male is the association o myocardial scarring from previous acute infarc tion. In this circumstance, the loss of muscl incident to healed as well as acute infarctio appears to favor pump failure.

In this study, scars of previous infarction wer found to be high, occurring in 64.5 per cent o all of the cases. Scars were common both i cases suffering electrical failure as well as pum failure with exception. This exception occurre in instances of rupture of the heart. Only one o ten cases with the latter complication showe myocardial scars. McQuay and associates[2] foun that in 60 per cent of fatal cases of acute myo cardial infarction there were scars of previou infarction.

In this study, the ratio of women to men wit rupture of the heart was 9:1. This ratio is out o line with larger studies. Nevertheless, the ab solute number of examples of rupture of th heart among the women in this study conforms t observations of other studies.[2] The nine example of rupture of the heart among the 28 wome of this study represent an incidence of about 3 per cent among fatal cases of acute myocardia infarction in women.

In keeping with observations of others regarding the incidence of coronary thrombosis,[3] this study showed a higher incidence of this lesion among subjects with acute transmural infarction (68 per cent) than in those with acute subendocardial infarction (35 per cent). Recently, consideration has been given to the question as to whether coronary thrombosis causes or follows acute myocardial infarction.[4,5] This study does not resolve the question. It is of interest, however, that among subjects with transmural infarction the incidence of coronary thrombosis was more common in those who survived from three to 14 days than in those who died before this period. This suggests support for the concept that coronary thrombosis may follow myocardial infarction. On the other hand, such a pattern was not noted among subjects with subendocardial infarction and coronary thrombosis.

Summary

The necropsy findings in 60 patients who had been admitted to a coronary care unit for acute myocardial infarction were correlated with the clinical states. In 48 instances, acute myocardial

infarction was confirmed pathologically. (In two of the 60 patients, death occurred about a month after admission. The pathologic study showed only healed infarction.) Of the 48 subjects with autopsy evidence of acute myocardial infarction, there were 20 male and 28 female subjects.

Thirty-five of the 48 cases had manifested pump failure and 13 electrical failure. In ten of the patients with pump failure rupture of the heart had occurred. Among the 48 cases, 31 had acute transmural infarction and 17 subendocardial infarction. Scars of healed infarction were observed in 31 cases (64.5 percent) but these were uncommon in cases with rupture of the heart.

The acute myocardial infarct was transmural in 75 per cent of the cases with pump failure and in only 39 per cent of the cases with electrical failure. Each of the cases with rupture of the heart exhibited transmural infarction. The ratio of women to men with rupture of the heart was 9:1. Acute transmural infarction was more common among the female patients; acute subendocardial infarction was more common in male subjects. Acute coronary thrombus was present in 56 per cent of the 48 cases with acute myocardial infarction. Among the cases with acute transmural infarction, 68 per cent showed acute coronary thrombosis, while the latter change was observed in 35 per cent of cases with acute subendocardial infarction. Among subjects with transmural infarction the incidence of coronary thrombosis was more common in those who survived for three to 14 days than in those who died two days or less following the onset of acute myocardial infarction.

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Say ye, oppress'd by some fantastic woes,
Some jarring nerve that baffles your repose;
Who press the downy couch, while slaves advance
With timid eye, to read the distant glance;
Who with sad prayers the weary doctor tease,
To name the nameless ever-new disease;
Who with mock patience dire complaints endure,
Which real pain and that alone can cure;
How would ye bear in real pain to lie,
*Despised, neglected, left alone to die?**

---

*George Crabbe; The Village, ll. 250-259, 1783.

The more physicians consider the hemodynamics of lowering blood pressure...

Most physicians now agree on the importance of reducing blood pressure in the hypertensive patient. But high blood pressure exists, of course, only as part of a complete clinical picture. The hemodynamic profile of well-established essential hypertension is characterized by elevated arterial blood pressure, normal cardiac output, and increased total peripheral resistance.

And so, physicians are increasingly concerned with the effects of an antihypertensive agent not only on blood pressure itself but also on the hemodynamic pattern—in short, with the total effect of the drug. *Does* it indeed help lower blood pressure effectively? *Is* peripheral resistance reduced? *Are* cardiac output and renal functions maintained? And, also, is there likely to be drug-induced postural hypotension serious enough to pose a threat to the patient's cerebrovascular status?

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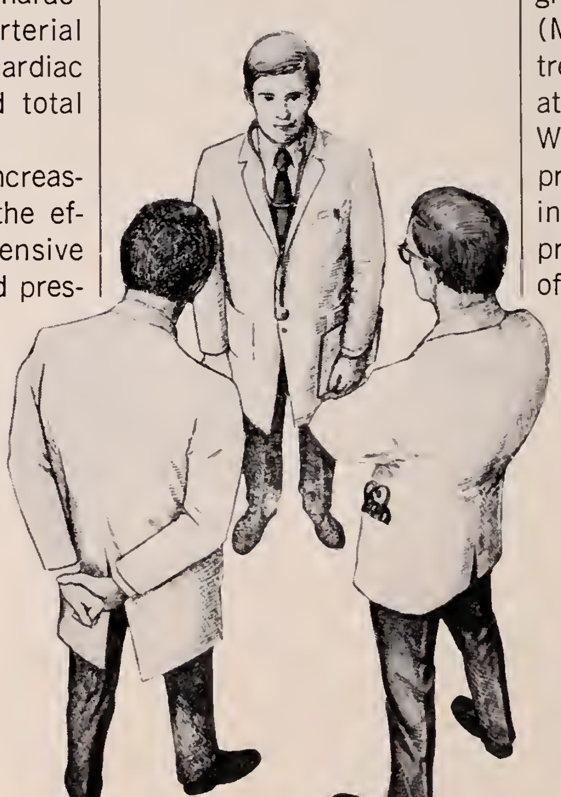
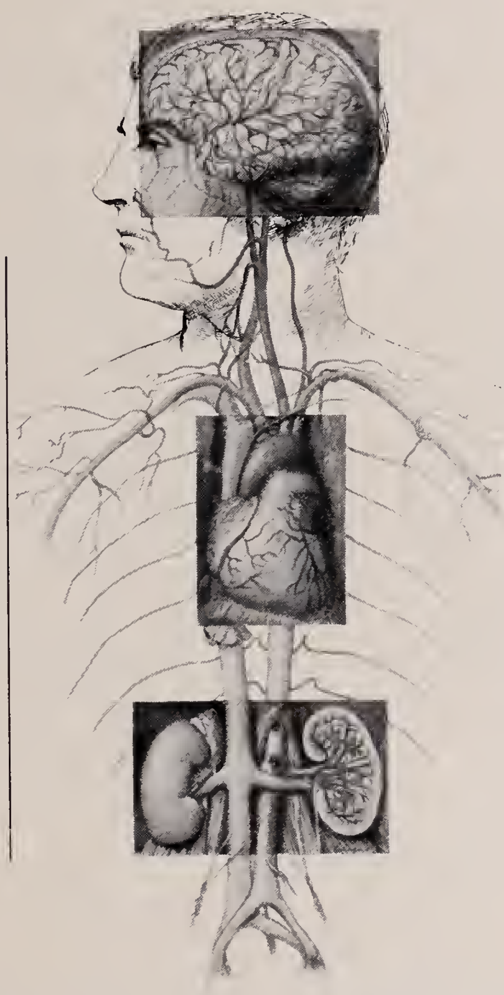


the more physicians rely on this unique antihypertensive



wering blood pressure. But ere are other considerations well. Cardiac output is usu- ymaintained with no cardiac celeration; in some patients e heart rate is actually owed. Peripheral resistance apparently reduced. DOMET does not usually mpromise existing renal nction; it generally does not duce renal blood flow, glo- erular filtration rate, or fil- ation fraction. And ALDOMET ually does not cause sympto- atic postural or exercise potension.

Contraindications include active hepatic disease and known sensitivity to the drug. Use with caution in patients with a history of liver disease or dysfunction. Not recommended in pheochromocytoma or pregnancy.

It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

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sustained moderate hypertension

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(METHYLDOPA MSD)

smoothly lowers blood pressure

Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis. Known sensitivity. Not recommended in pheochromocytoma. Unsuitable in mild or labile hypertension responsive to mild sedation or thiazide therapy. Use cautiously in patients with history of previous liver disease or dysfunction.

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between six and twelve months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at six and twelve months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first three weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first two to three months of therapy. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first six to twelve weeks of therapy or whenever an unexplained fever occurs. If fever, abnormalities in liver function tests, or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, reversible reduction in leukocyte count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur.

Use in Pregnancy and Childbearing Age—Not recommended in pregnancy. In women of childbearing age, weigh potential benefits against possible fetal hazards.

Precautions: Methyldopa may interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, spuriously high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has occurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: Sedation, usually transient, may be seen during initial therapy or when dosage is increased. Headache, asthenia, or weakness may be noted as early, transient symptoms. Symptoms associated with effective lowering of blood pressure are occasionally seen and include dizziness, lightheadedness, and symptoms of cerebrovascular insufficiency. Angina pectoris may be aggravated. Symptoms of orthostatic hypotension may occur; if symptoms occur, reduction of dosage is suggested. Bradycardia, nasal stuffiness, mild dryness of mouth, and gastrointestinal symptoms including distention, constipation, flatus, and diarrhea occur occasionally; these generally can be relieved by reducing dosage. Nausea and vomiting have been reported in only a few patients. Sore tongue or "black tongue," pancreatitis, and inflammation of salivary glands may occur.

Weight gain and edema occur infrequently and are relieved by administering a thiazide diuretic; if edema progresses or signs of pulmonary congestion appear, discontinue drug. A rise in BUN has been observed. Other rare reactions include breast enlargement, lactation, impotence, decreased libido, skin rash, mild arthralgia, myalgia, paresthesias, Bell's palsy, parkinsonism, psychic disturbances including nightmares, reversible mild psychoses or depression. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Note: Dosage should be limited initially to 500 mg daily when following previous antihypertensive agents other than thiazides. Maximal recommended daily dose is 3.0 g. Patients with impaired renal function may respond to smaller doses than patients with normal kidney function. Syncope in older patients has been related to increased sensitivity in those with advanced arteriosclerotic vascular disease; this may be avoided by lower doses. Tolerance occasionally seen either early or late, but more likely between second and third month after initiation of therapy; increased dosage or combined therapy with a thiazide frequently restores effective control.

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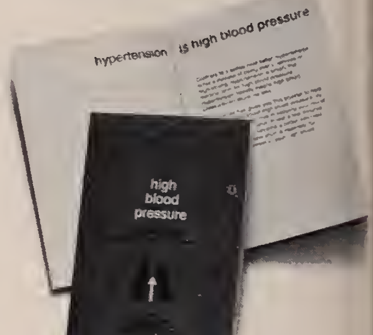

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Book Reviews

ETHICS IN MEDICINE IN A CHANGING SOCIETY. Edited by Stacey B. Day, M.D., Ph.D., D. Sc., Bell Museum of Pathobiology, 1973, 72 pages.

During January and February, 1973, the Bell Museum of Pathology, in the person of Stacey Day, put on a series of colloquia on "Society, Science, Civilization and Medicine." This thin volume contains the material on medical ethics which came out of three of those sessions.

If this symposium was less successful than its predecessor on *Death* and *Attitudes Toward Death* in 1972, the reason may lie in the fact that the subject has less universal applicability and impact-even for (nay, especially for) physicians. And if the book is less successful than a recent volume on the same subject edited by another former professor at the University of Minnesota, the reasons are multiple.

First, this is an edited transcript of three different sessions, not a series of essays. Dr. Day asked the questions and the responses came from as many as six different persons. This makes for lively, but disjointed exchanges. And when there are a lot of questions, as there are in the field of medical ethics, even good editing doesn't make for smooth reading or coherent presentation.

The second reason may lie in the make-up of the panel. Dr. Day described the discussants as being "of varying spectra politically, of many points of view, of different age groups, drawn from all levels of the faculty and student body." His description is accurate, but while such a mix will make for lively repartee and diverse ideas, it does not guarantee meaningful comment on, or even a fresher approach to, medical ethics. Indeed I have a feeling that one panel member had no idea what the subject meant and two other members intended to use their presence on the panels to espouse their own separate causes—neither which had anything to do with medical ethics.

Finally, it must be remembered that this book represents the proceedings of a symposium. As such it may be a good memento for those in the audience who were willing to allow themselves to be stimulated. But in its 72 pages there are so many questions, both in Dr. Day's formal questions and in the panelists answers, that the reader is left with the feeling that the whole thing is completely superficial. This feeling is heightened by the material on pages 65-72, which have nothing to do with medical ethics.

Stacey Day has left this part of the country. He will be remembered for many things—his questioning mind, his scholarship, his poetry, the symposium on death, and above all the imprint he has placed on the Bell Museum on Pathology. I think that Stacey Day could write a series of essays that would help his colleagues think their way through to a rational, humanistic schema of medical ethics. This book is not such.

Charles W. Jarvis, M.D.
St. Paul, Mn.

COMMENTS IN SPORT MEDICINE. Craig, T. T.: Chicago, American Medical Association, 1973. 230 pages, $5.00.

"Recommendations for sound health and safety practices in the care and supervision of the athlete" are the avowed objectives of this publication. The American Medical Association has compiled a group of pamphlets, published over the past 15 years, in the form of a practical and readable book for the athletic trainer, coach, or physician interested in the athletic pursuits. It is not an exhaustive medical treatise on sports problems but it is, instead, a series of useful suggestions in the care of the athlete. In keeping with current trends, there is even a two-page essay on the female athlete. I believe it should be recommended as a practical guide to the treatment of athletic problems, written in such a way as to be understandable to the lay person.

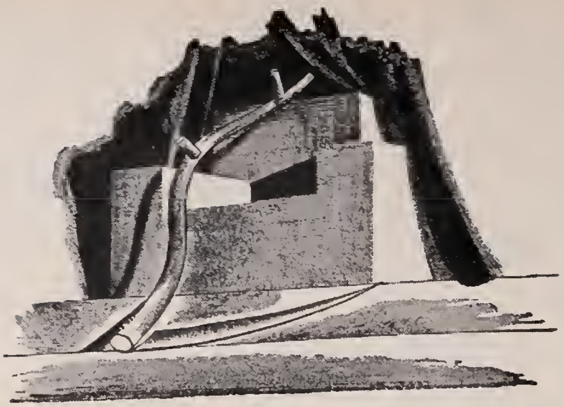
Kenneth A. Johnson, M.D.
Mayo Clinic and Mayo Foundation
Rochester, Minnesota

HANDBOOK OF SURGERY by John L. Wilson. Lange Medical Publications, Los Altos, California 1973. 878 pages. Cost: $7.00.

This fifth, paperbound edition of Surgery by Wilson is comprehensive and well-organized into 20 sections. It covers the various fields in surgery from Trauma to Organ Transplantation, and has within its numerous pages well-known authors such as Harper on Nutrition, Shumway on Heart and Great Vessels. Najarian on Organ Transplants, and John L. Wilson on General Surgery.

The Index, though not extensive, is adequate. Readability of the Handbook would be greatly enhanced with larger type, for certainly anyone whose vision is moving outward would become readily discouraged doing any extensive reading from a Handbook printed with six point.

Carl O. Rice, M.D., Ph.D.
Editor Emeritus



In Memoriam

ROBERT F. FISCHER, M.D.

Dr. Robert F. Fischer, 47, St. Paul psychiatrist, died July 31. He was a graduate of the University of Minnesota Medical School and was very active throughout the state in many medical organizations.

Born in Hibbing, Dr. Fischer upon completion of his medical education set up a practice in the Lowry Medical Arts Building in St. Paul. He was a member of the Ramsey County Medical Society, the American Medical Association and the Minnesota State Medical Association.

Dr. Fischer is survived by his wife, Lois, daughters Cynthia, Melissa and Leah and son, Robert.

HENRY HUTCHINSON, M.D.

Dr. Henry Hutchinson, 72, former superintendent at the Moose Lake State Hospital, died June 30. He was born in Akron, Ohio and obtained his medical education at the University of Minnesota.

Dr. Hutchinson was a member of the American Medical Association and St. Louis County Medical Society, a fellow of the American Psychiatric Association and an Associate Member of the Minnesota State Medical Association.

He is survived by his son, Richard.

WALTER G. NUESSLE, M.D.

Dr. Walter Nuessle, 85, Springfield physician, died July 7. His education was obtained at the University of Minnesota Medical School.

Dr. Nuessle was a member of the Brown County Medical Society and the American Medical Association and a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Nuessle is survived by his sons, Walter Jr., Dr. William, Ruth and Ursula.

HERMAN KESTING, M.D.

Dr. Herman Kesting, 91, St. Paul surgeon, died July 3. He had been practicing in the Riverview area of St. Paul for more than 60 years. Dr. Kesting was one of the organizers of West Side General Hospital, now Riverview Memorial Hospital. His medical education was obtained at Hahnemann College of Philadelphia.

He was a member of the Ramsey County Medical Society and the American Medical Association and a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Kesting is survived by his wife, Bess, and five daughters, Elinor, Elizabeth, Laura, Virginia and Julo.

JOHN P. MEDELMAN, M.D.

Dr. J. P. Medelman, St. Paul radiologist and Chief of Radiology at St. Joseph's Hospital since 1936, died July 6. He was a past president of the Minnesota State Medical Association and the American Roentgen Ray Society, secretary of the Minnesota State Board of Medical Examiners, a member of the American Board of Radiology, Ramsey County Medical Society, the American Medical Association and numerous other medical societies. In 1964 he was awarded the Outstanding Physician Citation by the Minnesota State Medical Association.

He was instrumental in getting the first cobalt therapy center in Ramsey County. Dr. Medelman is survived by his wife, Helen, and sons, John and James.

LEONARD J. MONSON, M.D.

Dr. Leonard Monson, 66, Canby physician, died July 7. He began his practice in Canby in 1937 where he built the Monson Clinic.

He was a member of the Lyon-Lincoln County Medical Society, the American Medical Association and the Minnesota State Medical Association.

Dr. Monson is survived by his wife, Eunice, son Dr. Bjorn Monson of St. Paul and two daughters, Mrs. Jon Lee and Mrs. Duane Monick.

C. L. OPPEGAARD, M.D.

Dr. C. L. Oppegaard, former Crookston physician, died July 6 in Scottsdale, Arizona. He was a past president of the Minnesota State Medical Association and winner of the 1962 Distinguished Service Award of that Association.

A University of Minnesota Medical School graduate, Dr. Oppegaard was also a member of the Red River Valley Medical Society and the American Medical Association and a Life and 50 Club Member of the Minnesota State Medical Association.

He was 76 years of age.

IN MEMORIAM

RALPH X. ROSSEN, M.D.

Dr. Ralph Rossen, 64, the first Minnesota commissioner of mental health, died June 27. He was appointed to the post in 1950 by Gov. Luther Youngdahl, and served about a year before going back to being director of the State Mental Hospital at Hastings. He remained director at Hastings until 1954. Later he became Director of the L. E. Phillips Fund for Psychobiological Research at North Memorial and Mt. Sinai Hospitals, a job he held until his death.

Dr. Rossen was a member of the American Medical Association, the Minnesota State Medical Association and the Hennepin County Medical Society.

He is survived by his wife, Beatrice, daughters Arlene and Mrs. Ricky Weiss.

OTTO B. FESENMAIER, M.D.

Dr. Otto B. Fesenmaier, 66, general practitioner, died May 19, at Pasadena. He had practiced in New Ulm before moving to California and had been the Brown County Coroner and Medical Director of the Minnesota Department of Health, Second District.

Dr. Fesenmaier was a member of the American Medical Association, the Brown County Medical Society and the Minnesota State Medical Association.

He is survived by his wife, Helene.

BENJ A. DVORAK, M.D.

Dr. Benjamin Dvorak, 78, Minneapolis surgeon, died May 3. He had attended the University of Minnesota Medical School and was a member of the Hennepin County Medical Society, the American Medical Association and the Minnesota State Medical Association.

Dr. Dvorak is survived by his wife, Beatrice, son, Dr. B. Anthony Dvorak of Phoenix, and daughters, Mary J and Betts.

S. PAUL EHRLICH, M.D.

Dr. S. Paul Ehrlich, 72, Minneapolis physician, died January 28. He was a graduate of the University of Minnesota Medical School.

In addition to being a Life Member of the Minnesota State Medical Association, Dr. Ehrlich was a member of the American Medical Association and the Hennepin County Medical Society.

He is survived by his wife, Dorothy, and sons, James F., Stephen A. and Paul Jr.

ELLERY M. JAMES, M.D.

Dr. Ellery M. James, pathologist in St. Paul, died May 29. He was 60 years old.

A graduate of Marquette University Medical School, Dr. James was a member of the Ramsey County Medical Society, the American Medical Association and the Minnesota State Medical Association.

He is survived by his wife, Ella, and sons, Ellery M. Jr., and William and daughters, Deborah and Mary.

JUSTUS OHAGE, M.D.

Dr. Justus Ohage, 88, St. Paul surgeon and former president of the Minnesota State Medical Association, died June 3.

He graduated from the University of Minnesota Medical School and studied two years at the Mayo Clinic in Rochester.

Dr. Ohage was a member of the American Medical Association and the Ramsey County Medical Society. In addition he was a 50 Club and Life Member of the Minnesota State Medical Association.

He is survived by his wife, Esther.

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convulsant medication; abrupt withdra
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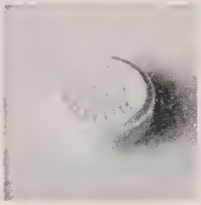
For further information on this subject, the following references are provided:

1. Henry BW, *et al: Dis Nerv Syst 30*:675-679, Oct 1969.
2. Hollister LE, *et al: Arch Gen Psychiatry 24*:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics 11*:438-441, Sept-Oct 1970.



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President's Letter

Under My Skin

THERE ARE FEW things that really arouse my ire. But the continued return of the politician to the concept of medicine as a public utility has disturbing implications for us and for our patients. Area franchising, rate control, and eventually location of types and numbers of physicians are all included in this concept. We all accept the idea that medical care is a right of the individual, but does this necessarily justify the adoption of the public utility approach? For this approach implies that people are all alike, the same shape, size, mentality, and emotional makeup. We meter water by the cubic foot and electricity by the kilowatt hour, so we then can expect people as a constant unit from the pipe or wire, denying them their rights of individuality.

Without question, mechanically, a better system of delivery can be evolved. One need only look at or recall one's army service to know that a truly mechanical system was developed. By most standards army medicine was of good quality. By any humanistic standard, it left much to be desired. Paramedical personnel were efficiently used. All of us who served in the army were impressed with the dispensory sergeant and the way he made the sick call lines disappear. The patient ran the paramedical gauntlet before seeing the doctor. We all realize that truly sick people and even slightly sick people do not want someone else deciding when or whether they should see their doctors.

Recently great publicity has been given to patients' rights by consumer advocates, as if common courtesy had not been afforded the patient by his physician. Concern for the patient as an individual has long been the doctor's creed.

Now we have a group of people trying through the legislature to plan controls over the delivery system which will weaken the patient-doctor relationship, something that they have been discounting for a long time.

Under the latest plan to be presented to the Minnesota State Legislature, there will be created a Health Service Policy Board consisting of thirteen members, one of whom will be a licensed medical doctor. This board will have sweeping control over the medical field. It will issue certificates of need, review rates, approve contract and financial arrangements between health care facilities and physicians who provide service, issue licenses to health care facilities, conduct investigations, audits, and inquiries, promulgate rules and regulations, and finally exercise all other powers which are reasonably related to effective implementation of this act.

The Metropolitan Health Board with only the power of certificate of need has had great impact on medicine and the way it is practiced. One can only be concerned with the added powers invested in this proposed governor appointed board.

All persons in the field of health must arise to this challenge. The State Medical Association cannot alone respond to this proposal. We need the input of the individual physician through his state legislator.

Dr. Henry E. Michelson, to whom this excellent issue of Minnesota Medicine is dedicated, was an outstanding physician and scholar who set his own high standards of practice and teaching. His was a tradition of self-discipline, and independent thought, a way of practice becoming increasingly difficult with present day controls.

Bernard Hall M.D.

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Nephro-Urologic Seminar

October 18-19—Mayo Clinic—Contact: Mr. W. L. Nietz, Mayo Clinic.

Outside Rochester

Faribault Medical Seminars

October 12, Faribault,,—"G.I. Bleeding"—Contact: Roy H. Good, M.D., Faribault Clinic.

Fergus Falls Medical Seminars

October 18-19, Fergus Falls, Minnesota—"Cardiology"—Contact: Mehdi Orandi. M.D., Lake Region Hospital.

Goodhue-Wabasha County Medical Seminars

October 28, Red Wing, Minnesota—"Collagen Disease & Rheumatoid Arthritis." Contact: R. V. Sherman, M.D., Interstate Medical Center.

Owatonna Medical Seminars

October 14, Owatonna, Minnesota—"Alergies"—Contact: Mr. Howard Place, Owatonna City Hospital.

Hibbing Medical Seminars

October 16, Hibbing, Minnesota—"Neurology"—Contact: R. E. Hanson, M.D., Hibbing General Hospital.

Minnesota Society of Internal Medicine

Semi-Annual Meeting, Saturday, October 19, 8:00 a.m., in St. Paul. Contact: Mahlon Burbank, M.D., Mayo Clinic, Rochester.

Southwestern Minnesota Medical Society

"Common Problems in Pediatric Dermatitis" October 7, 8:00 p.m., Michaels Steak House, Worthington. Contact: E. S. Boone, M.D., 215 No. Cedar, Luverne, Mn.

University of Minnesota

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Internal Medicine Review—October 1-5, 1974

Specialists in Internal Medicine planning to take the recertification examination may be helped in their preparation by a systematic review based on the A.C.P. *Syllabus.*

Application of Computers to the Clinical Practice of Medicine—October 3-5, 1974

The Department of Laboratory Medicine together with the Society for Computer Medicine join in a new area of increasing interest to practicing physicians.

Miller-Dwan Medical Center Foundation

Symposium on Hypertension, Miller-Dwan Auditorium, Friday, November 1, Duluth. Contact: A. J. Houglum, M.D., Miller-Dwan Hospital.

9:00 A.M.	WELCOME Donald B. Shank, President, Miller-Dwan Medical Center Foundation Edward Ryan, M.D., President, Minnesota Heart Association.
9:10-10:00	WHAT IS HYPERTENSION, AND WHY TREAT IT? Ray W. Gifford, Jr., M.D.
10:00-10:45	INITIAL EVALUATION OF THE HYPERTENSIVE PATIENT John A. Spittel, Jr., M.D.
11:00-12:00	LOW-RENIN HYPERTENSION James C. Melby, M.D.
12:00-12:45	RADIOLOGIC DIAGNOSIS OF HYPERTENSION Mahlon H. Burbank, M.D.
2:00- 3:00	SURGICAL TREATMENT OF HYPERTENSION Phillip Bernotz, M.D.
3:00- 3:45	MEDICAL TREATMENT OF HYPERTENSION Ray W. Gifford Jr., M.D.
4:00- 5:00	PANEL-CASE PRESENTATIONS: PROBLEMS IN HYPERTENSION Moderator: James C. Melby, M.D.

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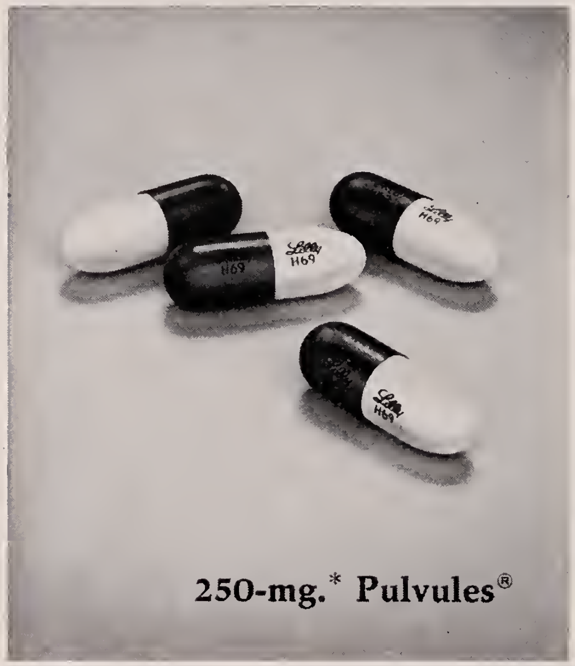

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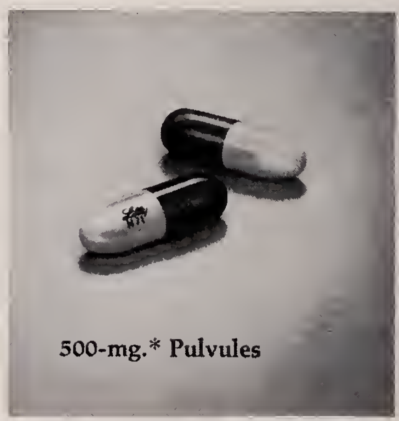

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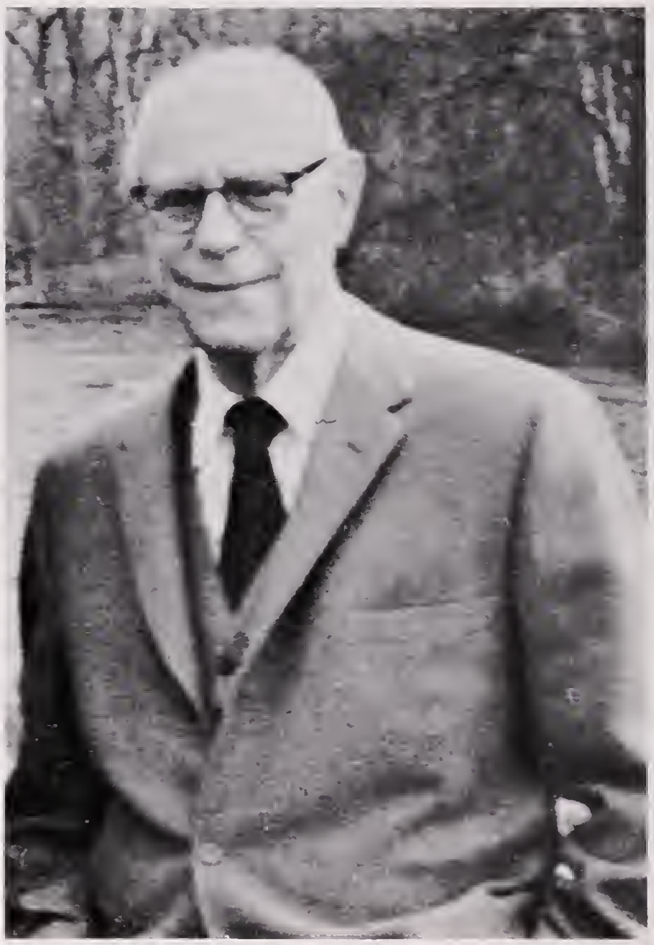

Henry E. Michelson, M.D.
1888-1972

Editorials

This Dermatologic Issue

This Dermatologic issue of Minnesota Medicine is dedicated to the late Dr. Henry E. Michelson, who was Professor and Head of the Division (now Department) of Dermatology, University of Minnesota, 1925-57. Dr. Michelson was nationally and internationally regarded as an honored practitioner, teacher, writer, creative thinker, a leader in medicine, and as a man of great personal and professional integrity. His greatest contribution, however, was his unique ability to communicate insights into disease processes with clarity and simplicity to students of all stages. He would have enjoyed the subjects and content of these articles, which present new, useful information for clinical practitioners.

This is a dynamic time in American dermatology. The departments of dermatology are energetically and successfully fulfilling the important responsibilities of teaching medical students, residents, and fellows, and of continuing education of dermatologic and non-dermatologic physicians. In dermatology, as in all fields of medicine, there is a great need for continuing education. The Academy of Dermatology has expanded its role as a fulcrum for the continuing education of dermatologists. The National Program for Dermatology (NPD), a planning arm of the Academy, has since 1968 occupied itself with creative planning and program development for the future. The Dermatology Foundation is engaged in developing financial resources from within the specialty and from outside sources. The National Program is served by 450 dermatologic volunteers (one in eight of all dermatologists). Weary,[1] has summarized some of the recent activities of the NPD which include: a placement bureau for dermatologic practitioners, a placement bureau for academic manpower, contact dermatitis patch test kit, collation of national health survey data, postgraduate symposium at the American Medical Association meeting, science writers and beauty editors symposium, development of educational programs for schools, basic science teaching series, completion of a self-assessment examination and home study course project.

The lead article of this issue*—"Cutaneous Signs of Internal Malignancy"—by Dr. Walter B. Shelley, Professor and Chairman, Department of Dermatology, University of Pennsylvania, was presented in part as the dedication lecture on the occasion of the first Henry E. Michelson Clinical and Scientific Seminar, May 17-18, 1974. The other articles were presented in Minnesota in 1974, some at the spring refresher of the Minnesota Academy of Family Physicians, others at the Continuation Course ("Clinical Dermatology for Family Practitioners") of the Department of Dermatology and Office of Postgraduate Medical Education, University of Minnesota. Each of the authors is an authority in his field of presentation.

I wish to thank the contributors for their excellent articles and the Board of Editors of Minnesota Medicine who presented the invaluable use of color for the dermatological illustrations.

Milton Orkin, M.D.†
Guest Editor

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†Clinical Professor, Department of Dermatology, University of Minnesota Hospitals.

*See page 773.

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1. Weary PE: The National Program for Dermatology. Archives of Dermatology 109:499-501, 1974.

Diseases of the Skin

Everybody sees diseases of the skin. This issue considers particularly those that are common and turn up in every physician's practice. Dr. Milton Orkin, guest editor, selected these universal topics in dermatology. Certainly at one time or another every physician has been asked his advice on what to do for common baldness. A reprint of Muller's papers* will provide a ready and authoritative answer. Schorr† has some practical points for the general physician who must take care of contact dermatitis.

Two papers are concerned with oncology: Shelley‡ makes the point that a careful skin examination may discover clues to a cryptic internal cancer. Lynch# describes the tumors one encounters primarily in the skin.

Henry Michelson, to whom this issue of Minnesota Medicine is dedicated, is remembered by Minnesota medical graduates of the last half century. He was of course a master in his field. He was also a master teacher. Standing in the pit of Eustis or Todd amphitheaters in the University Hospital facing the junior or senior class he would describe a medical illness with dermatologic manifestations in words forever committed to memory and in unforgettable style. His interest was in the total disease and never confined to its effects on the skin. I recall early in my practice a consultation on a patient with dermatomyositis. Michelson was the attending and I was the consultant. After my examination I sat down with Henry to discuss the medical aspects of the case. Dermatomyositis at that time was not a disease whose medical aspects were fresh in my mind and I had taken the precaution to prepare for this dialogue by reading everything I could lay hands on about this disease. Michelson had read every reference I could quote and our dialogue became a great clinical presentation by the master for one student. Minnesota became a great medical school during the last half century and Henry Michelson contributed significantly to its reputation.

Diagnosis of skin disorders is first and last a visual effort. No journal can do justice to skin pathology in black and white. This issue is lavishly illustrated in color thanks to financial aid given to Minnesota Medicine by several pharmaceutical firms.§

Reuben Berman, M.D.
Editor

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*See page 809.
†See page 831.
‡See page 773.
#See page 780.
§Reed and Carnrick and Dermik Laboraotries, Inc.

Cover Photo

"Lake Louise"

Dr. David Gauger, a resident in pathology at Hennepin County General and the University of Minnesota Hospitals, took the cover photo while on vacation in Western Canada. He used a Nilsen FTN camera with Kodachrome film.

Dr. Gauger grew up in Early, Iowa, and attended the University of Iowa College of Medicine. He interned at Hennepin County General Hospital and is presently on the Berry Plan in Anatomic and Clinical Pathology. He will enter the Air Force as a pathologist in January of next year.

Continuing Medical Education

(continued from page 767)

Association of Minnesota Internists

On Wednesday, October 30, 1974, the Association of Minnesota Internists will be holding a General Membership Meeting at the Sheraton Motor Inn. Social hour at 6:30 p.m. followed by a brief meeting. The program for the evening will be a panel to discuss 'The Next Ten Years In Internal Medicine'.

Wilder Child Guidance Clinic

Wilder Child Guidance Clinic Symposium. Five nationally known child mental health Speakers. October 11, 9:00 a.m., St. Paul Athletic Club. Information: 645-6661.

St. John's Hospital

Bill Pew, M.D. and Miriam Pew, ASCW, Directors of the St. John's Hospital Family and Marriage Education Centers, will present a course entitled, "Is Harmonious Living Possible," in four two-hour sessions beginning October 30 at St. John's, 403 Maria Ave., St. Paul.

Sessions also will be held on November 6, 13, 19.

Cost: $3 per session.

Cutaneous Signs of Internal Malignancy

WALTER B. SHELLEY, M.D., Ph.D.*

To have been invited to give the First Michelson Memorial Lecture is a high honor indeed for anyone, but for me it is an especially treasured accolade. For, it was as a student in the Class of '43 here at Minnesota, that I came under the magnetic influence of Henry E. Michelson, and hence into my career in dermatology. Michelson was a man whose stature must be measured in many dimensions. But with me the picture will always remain that of the master teacher. Thirty patients were brought before all one hundred and twenty-five of our Junior class every Friday afternoon from 1:00 to 2:00 in an amphitheatre. Each exemplified a singular diagnostic or therapeutic point Michelson wanted to make. Each remained in the hall outside for the second hour where we would file by at close range to reinforce and to review those precious points Michelson had made. His quiet incisive "patient-side" teachings imparted to us a clinical confidence we found in no other field. All of us turned Seniors, the better for our Friday hours with Michelson.

In the case of any unexplained skin change the patient thinks of internal malignancy first—and the physician thinks of it last. Indeed neither the latest treatise on cancer medicine,[1] a magnificent 1973 tome of 2018 pages, nor the classic four volume encyclopedic work of Wolff on the same subject initiated in 1907,[2] mention the skin as a marker of internal cancer (Figure 1). Yet physicians are aware of the growing importance of radio-immunoassay of the wide spectrum of antigenic and hormonal products elaborated by tumors[3] (Table) all dramatized by the recent commercial introduction of the carcino-embryonic antigen (CEA) test for cancer.[4] They recognize that enzyme changes in the blood may herald cancer and there is no one unaware of the radiologic armamentarium in detecting cancer, to say nothing of the direct signs and symptoms of cancer as perceived by the clinician. But what are the clinical signs in the skin that should alert not just the patient but the physician himself to think of cancer within?

The signs are real, but they are rare. Even though inspection of skin changes must be one of the most rapid of non-invasive screening programs, you have to look, think and imagine. You have to listen to the patient. Often the signs sneak by if you but nod in a moment of "end

Fig. 1—No information on the cutaneous signs of internal cancer is provided by these definitive works on cancer medicine, dating from 1907 to 1973.[1,2]

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*Professor and Chairman, Department of Dermatology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.

Given as the first Henry E. Michelson Memorial Lecture at the University of Minnesota, Minneapolis, Minnesota, May 18, 1974.

of office hours" fatigue. These signs are not precise, fixed or unique, and most are caught by the physician with an unfailingly high index of suspicion. He has a suspicion that is sharpened by a continued awareness that the unexplained, the strange, the atypical, may be induced by internal cancer.[5-10]

But specifically what are these signs of the skin that demand not reassurance, but re-examination of the patient? They are indeed a motley multivariate lot. Some are so rare as to force the clinician to be anecdotal or agnostic. Others are so commonplace as to be ignored. None is as precise, diagnostic and recognizable as a wart. Many can only bring up the haunting possibility of internal cancer. Since I cannot put them in tidy divisions, I shall group them as to their impact on us as physicians: The Dramatic, The Bizarre, The Puzzling, The Commonplace, The Disturbing and The Distinctive.

TABLE

Antigenic products of tumours for which radioimmunoassays have been described

Antigenic products	Associated tumours	References
Fetal antigens α-Fetoprotein	Hepatoma; teratoma; endodermal sinus tumour; hepatic metastases from gastric carcinoma	See Text
Carcino-embryonic antigen	Carcinoma of gastrointestinal tract, pancreas, gallbladder, lung, breast, ovary, testis, prostrate, cervix, bladder, kidney	
Placental antigens Human chorionic gonadotrophin	Trophoblastic tumour of placenta; teratoma; seminoma; insulinoma; melanoma; hepatoma; carcinoma of bronchus, breast, pancreas, gastrointestinal tract	
Human placental lactogen	Carcinoma of bronchus; in 8% of a variety of other tumors; trophoblastic tumors	
Placental alkaline phosphatase	Carcinoma of bronchus, bile ducts and others	
Peptide and glycoprotein hormones Corticotrophin	Carcinoma of bronchus, thymus, breast, pancreas, thyroid, liver, prostate, ovary	O'Riordan, Blanshard, Moxham & Nabarro (1966); Besser & Landon (1968); Liddle, Nicholson, Island, Orth, Abe & Lowder (1969)
Follicle-stimulating hormone	Carcinoma of bronchus	Faiman, Colwell, Ryan, Hershman & Shields (1967)
Antidiuretic hormone	Carcinoma of bronchus, pancreas, duodenum	Liddle et *al.* (1969)
Thyroid-stimulating hormone	Carcinoma of bronchus; choriocarcinoma	Hennen (1967); Odell, Hertz, Lipsett, Ross & Hammond (1967)
Prolactin	Carcinoma of pituitary, bronchus, kidney	Turkington (1971)
Growth hormone	Carcinoma of bronchus	Glass, Russell & Davies (1972)
Gastrin	Zollinger-Ellison syndrome	Gregory, Grossman, Tracy & Bentley (1967); Friesen, Bolinger, Pearse & McGuigan (1970)
Insulin	Carcinoma and adenoma of pancreatic β cell	Marks (1971)
Glucagon	Carcinoma of pancreatic α cells, bronchus, kidney	Unger, Lochner & Eisentraut (1964)
Renin	Wilms' tumour; haemangiopericytoma	Lee (1971); Spergel & Ertel (1972)
Thyrocalcitonin	Medullary carcinoma of thyroid	Cunliffe et *al.* (1968); Baylin, Beaven, Keiser, Tashjian & Melvin (1972)
Parathyroid hormone	Carcinoma of bronchus, kidney, ovary, endometrium, breast, cervix, vulva, pancreas, oesophagus	Berson & Yalow (1966); Melick, Martin & Hicks (1972)

Copied from K. D. Bagshawa's paper, Tumour Associated Antigens, Brit Med Bull. 30:68-73, 1974 (by permission).

The Dramatic

The early students of skin disease failed to even conceive of internal cancer as a cause of skin disease. The relationship of a tumor to the skin was far more subtle and difficult to perceive than that of the scabietic mite or the pathogenic fungus. Only by seeing "dramatic unforgettables" did the observers begin to sense that the skin could indirectly display a cancer within.

Acanthosis Nigricans was just such a dramatic change to excite the curiosity of all. It was the evening star of this field and was recognized by 1893 as a sign of internal malignancy.[11] And generations of physicians have recapitulated the history of medicine in their own training by becoming aware of it (Figure 2). Now that over 500 cases have been described we have learned that this velvety black warty growth is not an invariant sign of cancer. It may be the associate of endocrine disease, an overdosage of estrogens or nicotinic acid, or genetic abnormality.[12] Yet in one of every five, cancer may still be found.

Dermatomyositis is an equally dramatic syndrome of muscle weakness and pain with inflammatory skin plaques and swollen heliotrope eyelids (Figure 3). By 1916 it was hailed as a marker of malignancy. Today we find that at least half of the patients past the age of 40, who develop dermatomyositis, have a malignant neoplasm.[13] Dermatomyositis thus demands the most careful, prolonged, detailed study of the patient for malignancy. The ovary and breast, as well as the bronchus and stomach, are prime suspects. A form of immune hypersensitivity is held responsible since the skin of the patient is uniquely reactive to extracts of the tumor. Once the tumor is excised the signs of dermatomyositis disappear. Conversely if it is not recognized and removed, the tumor, the skin and the muscle changes proceed along an inexorable, fatal course. Another unforgettable sign of malignancy is the sudden appearance of downy hair over the face and body (Figure 4). First described in 1865 in a woman suffering from carcinoma of the breast,[14] it remains truly a rarity with only nine recorded examples.[15] Interestingly in this *Hypertrichosis Lanuginosa,* the papillae of the tongue which are pilary analogues, also show enlargement, thus also responding to an unidentified chemical stimulant secreted by the cancer. The serum of such patients surely holds the key to greater understanding of the body's hormonal controls.

Fully as dramatic but far less specific are the *Bullous Eruptions* which herald the presence of malignancy[16] (Figure 5). These usually skirt the well defined entities of pemphigus, pemphigoid, and dermatitis herpetiformis. It is their atypicality that gives the clinician the greatest urge to seek out an occult malignancy. The bullae may be flaccid, even inapparent, suggesting pemphigus erythematodes. In all instances the bullous eruption calls for internal diagnostic study since it can be the result of an immune mechanism rejecting an antigen common to the entodermal bowel tumor and the ectodermal epidermis. Such an antigen may be released in large amounts following radiation therapy, and this accounts for the subsequent erythema multiforme-like rashes.

No less remarkable are the rings, whorls and polycyclic waves of migratory inflammatory change as a result of internal tumors. Figure 6 shows an example associated with massive breast hypertrophy.[17] These are the *Figurative Erythemas,* with erythema gyratum perstans as one of the most amazing of these immune markers of cancer.[18]

Possibly the most arresting of all the signs is that of *l'homme rouge,* the patient with his entire skin a fiery red with inflammation (Figure 7). Such an erythrodermic *Exfoliative Dermatitis* is a relatively frequent manifestation of lymphomas and leukemias, but a definite yet rare marker of cancer itself.[19]

The Bizarre

The bizarre and inexplicable must always suggest the possibility of an underlying malignancy. Nearly always the eruption is exceedingly rare, the "once in a lifetime" case. *Reticulohistiocytoma, Pachydermoperiostosis* and *Erythema Elevatum Diutinum* are examples where strange plaques or enlargement of hands point to malignancy. Likewise the ulcers of *Vaccinia necroticans, Necrotizing Vasculitis* and *Ecthyma Gangrenosum* alert us to immune or bacteremic states which may coexist with malignancy.[20-22] *Recurrent Thrombophlebitis* is yet another signal to heed. *Plane Xanthoma* appearing as a gigantic xanthelasma extending over large areas of the body, may be the sign of multiple myeloma.

The Puzzling

But not all of the signs are rare. Some come

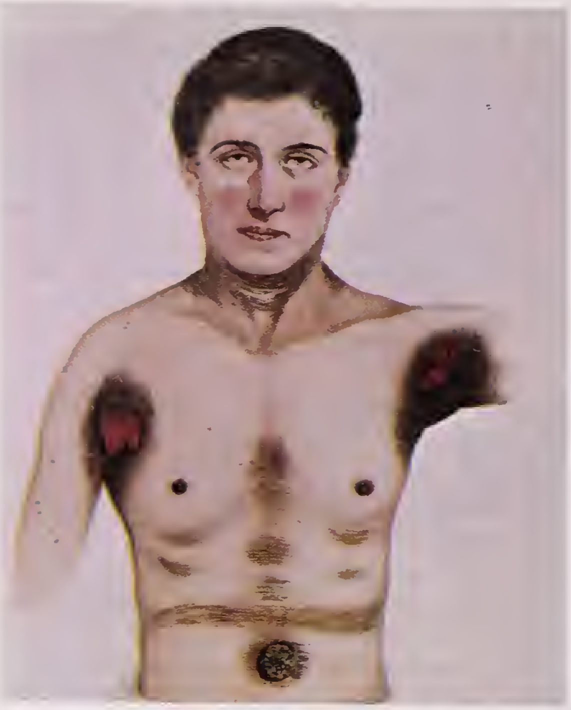

Fig. 2—This 1894 portrait of acanthosis nigricans served as a teaching model for years. The patient was a woman whose loss of hair and later demise were also believed due to an internal malignancy.[11]

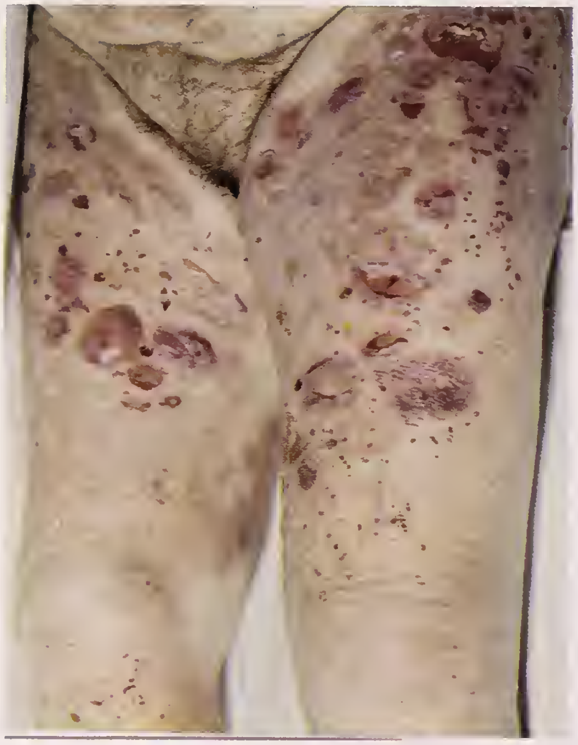

Fig. 5—Study of this patient's bullous eruption led to discovery of adenocarcinoma of bowel. Successful resection followed by disappearance of eruption. Reappearance years later heralded a recurrence of the adenocarcinoma.

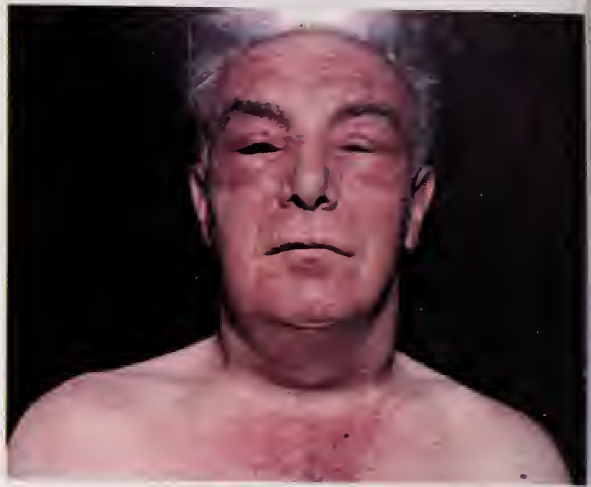

Fig. 3—Dermatomyositis. This man's dermatitis and muscle weakness were traced too late to an inoperable cryptic cancer of the esophagus.

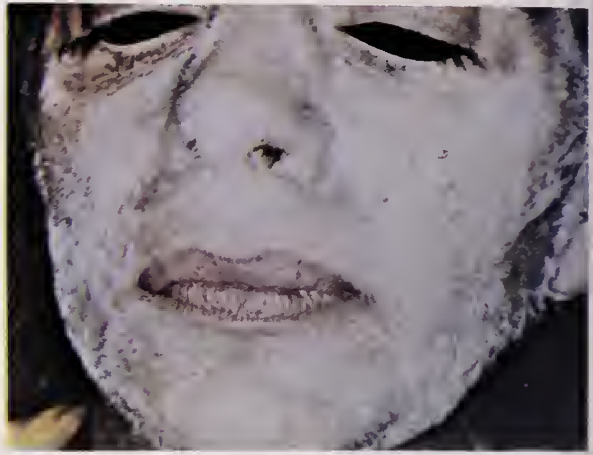

Fig. 4—This is the portrait of hypertrichosis lanuginosa as published by Hegedus and Schorr.[15] The fine long silky lanugo hair developed suddenly in a woman of 45 who had an adenocarcinoma of the colon.
(Arch Dermatol 106:84, 1972—Copyright 1972, American Medical Association, permission granted to reproduce.)

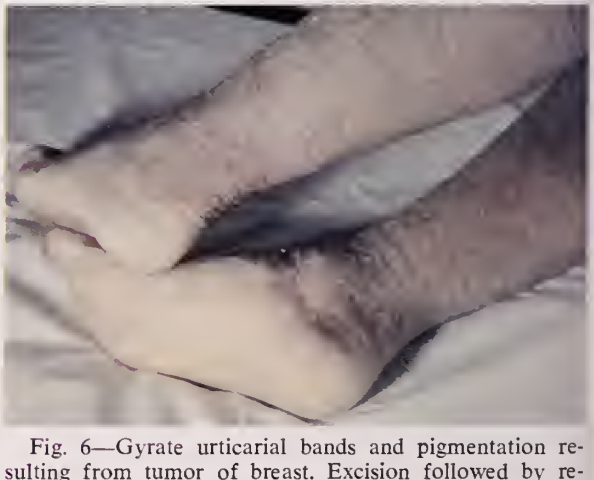

Fig. 6—Gyrate urticarial bands and pigmentation resulting from tumor of breast. Excision followed by remission.

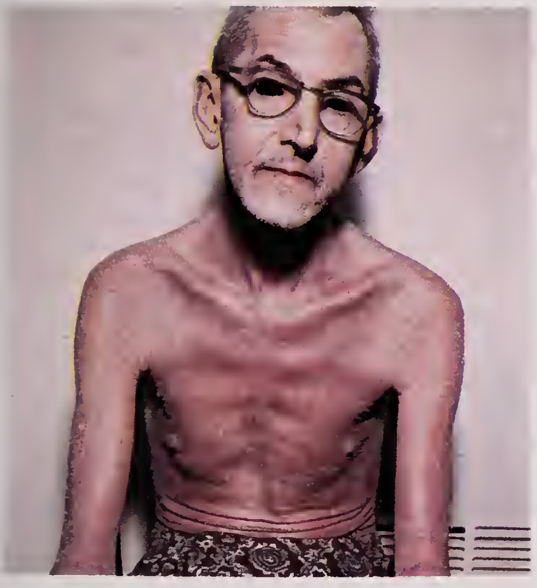

Fig. 7—Exfoliative dermatitis due to leukemia.

in the guise of the puzzling complaint. Often we have only the patient's description, the objective findings are vague, debatable. It is in this framework that we must listen to the patient, and proceed with studies for malignancy. We must respect the fact that a patient's awareness of "ill-being" still far exceeds the physician's capacity to detect it. Listen and study the patient who complains of a *Fixed Erythema, Clubbing of the Fingers, Gynecomastitia, or Swelling of the Face* in the morning. *Episodic Flushing,* even if you haven't seen the patient in an attack, may result from vasoactive compounds elaborated by a malignant carcinoid of the bronchus or gut. Don't ignore what you can't see, what you can't explain. In at least one elderly patient the trail went from sunlight intolerance to porphyria, and finally to a hepatoma.[23] In another a spate of varices on the abdomen heralded an underlying ovarian tumor. Believe the patient and look for cancer.

The Commonplace

Although the dramatic, the bizarre and the puzzling may pique the physician into looking for cancer, an even larger group of equally important signs may be dismissed as trivial. These are the commonplace signs which may have cancer as an uncommon cause.

None can be missed or misinterpreted more easily than the hallmark of cancer itself, the *Metastasis.*[24] In a busy practice, in the rush of rounds, or overshadowed by a major complaint, a solitary nodule of the scalp, umbilicus (Sister Joseph's nodule), or scrotum can pass unchallenged as an insignificant cyst. Even more inapparent may be the metastases to the conjunctival mucosa, or the one simulating a bunion. Even trauma may be a localizing factor. Only the biopsy scalpel and a prepared mind can bring us to the truth. A pulsatile nodule should make us envision a metastatic hypernephroma, not a vascular anomaly. A *Cellulitis* of inapparent cause deserves biopsy for it may be the manifestation of metastases. Metastases may also mimic the garden variety *Pyogenic Granuloma* or a patch of *Morphea,* at times with hair loss. Be prepared to see these clones of cells in their varied masquerades within the skin and know and prove them for what they are. The patient may not point them out. You must look closely.

Not only do malignant tumors metastasize to the skin, but they subtly interfere with the body economy, its chemistry, its function. And on this rests all the commonplace signs. In the epidermis the keratinocyte, melanocyte and free nerve endings are affected. From this springs the most significant yet oft ignored sign of cancer, i.e. *Pruritus.* No patient with unexplained itch can be presumed to be free of malignancy. Time and again an itch is considered psychogenic only to be the prodromal symptom of Hodgkin's disease or malignancy elsewhere.

Another commonplace sign induced by cancer is dry skin. Nothing could be more common—but we should use our diagnostic fire power for the individual over 40 who describes a sudden onset of this *Acquired Ichthyosis.* A similar but more focal sign is the precipitous onset of *Keratosis Pilaris.* A search for cancer in these individuals can be more rewarding than the recommendation of Nivea® cream.

Although the darkening of skin in cachectic, cancer ridden individuals has been known since earliest medicine, only now do we perceive the significance of ectopic MSH and ACTH-like production by tumors and its induction of localized and diffuse brown *Melanosis* via the melanocyte. A tan of uncertain origin deserves further study. Equally significant but more obscure, is the fact that tumors may be associated with loss of melanocyte function as in *Vitiligo*.

Of the epidermal derivatives the hair is the most responsive to the hormonal changes that may come with malignancy. We are all aware of the *Hirsutism* that bespeaks an ovarian or adrenal tumor. More difficult to assess is the *Diffuse Thinning of Hair* the patient may experience. Here, recall that women may lose over half their hair without it being evident to the new observer. Her history cannot be ignored. More obvious are the patchy areas of *Alopecia Mucinosa,* the sign of reticulosis. *Anhidrosis* is also associated with malignancy such as multiple myeloma, but its objective assessment is more difficult and not often undertaken.

The vessels are not exempt and changes here contribute much to the commonplace signs uncommonly seen as due to cancer. Persistent, unexplained *Urticaria* invariably raises the question of underlying malignancy, as does *Purpura,* whether it be thrombocytopenic or the result of the infiltrates of multiple myeloma. *Anemia* and *Jaundice* are two other cutaneous physical signs in the skin long in the lexicon of the cancer detective.

Strangely, even commonplace dermatologic diseases may signify cancer under special conditions. *Herpes Zoster* in the child or immunologically mal-competent adult may be the first sign of lymphoma or cancer. Similarly the sign of Leser-Trélat (the sudden appearance and rapid growth of *Seborrheic Keratoses*) has been associated with cancer. Recurrent recalcitrant *Pyoderma* alerts us to the possibility of leukemia. Another common finding, *Eczema of the Nipple,* may be Paget's sign of adenocarcinoma of the underlying breast, just as seepage induced *Pruritus Ani* can clue us into an adenocarcinoma of the rectum.

Internal malignancies also seem capable of inducing what might be called *para-dermatoses.* Thus, unusual forms of *Psoriasis,* aberrant versions of *Pityriasis Rosea,* distortions of *Lichen Planus,* as well as pustular and other analogues of *Dermatitis Herpetiformis* have all been construed to relate to internal malignancy.[9] It is a fascinating story of the interplay of these diseases in a soil unquestionably altered by the presence of cancer elsewhere.

The Disturbing

Not all of the "malignant signs" we read in skin are those of the present. Some are a portent. These are the disturbing ominous signs of cancer to come.

Thus in our reading of the *Palmar Keratosis* of patients exposed to arsenic, we can see a frightening future of possible cancers of the larynx, lungs, esophagus, liver and bladder.[25] Diffuse *Keratoderma* of the palms and soles raises the question of a familial trait leading to esophageal carcinoma eventually.[26] The melanotic macules of the lips and or face in *Peutz-Jeghers* syndrome may portend malignant change in polyps of the stomach and duodenum. The massive *Keratinous Cysts* of the face and chest of Gardner's Syndrome are signs of premalignant polyps of the colon. And to further inter-relate skin and gut, *Dermatitis Herpetiformis* gives augury of future increased risk of lymphoma or carcinoma of bowel. Most recently large multiple *Sebaceous Adenomas* have been associated with multiple visceral carcinomas especially of the colon.[27]

In the superficial inflammatory epidermal tumor of *Bowen's Disease* we read of a systemic carcinogenic process. This same process will eventually induce clinically identifiable malignancies elsewhere in the body. Equally alarming are the fibromas, axillary freckling, and other cutaneous signs of *von Recklinghausen's* disease. Nearly one in three of these patients will develop malignant schwannomata as the years pass into decades.[28]

Of even sadder and graver import is the reading of cutaneous signs of immunodeficiency states in children.[29] It is these infants with the *Mongolian Spots* of Down's disease, the *Pigmentation* of Fanconi's syndrome, the conjunctival and cubital *Telangiectasia* of ataxia telangiectasia, the *Photosensitivity* of Bloom's syndrome or the *Eczema* and *purpura* of Wiskott-Aldrich syndrome that are early heirs to lymphomas, leukemia and malignancy.

The Distinctive

Although all of the signs we have reviewed disappointingly are non-specific and only vaguely suggestive of internal malignancy, the physician does have a solitary boast. He can now recognize a distinctive, definitive dermatosis specifically associated with alpha cell tumors of the pancreas. Such a precision diagnosis of a specific, operable, internal tumor can lead to the prompt cure of an otherwise fatal disease. How is it done?

The diagnosis is based on an awareness of the remarkable necrolytic changes induced in the epidermis by the circulating products of the pancreatic alpha cells.[30] Presumably this may be glucagon, a compound that now merits intense study by students of the epidermis. In any event, the patient's eruption is an intractable yet remittent superficial eczema. It has a gyrate patterning but remains as an ill defined dermatitis until one grasps the essential feature that the outer epidermis rubs off as in a very superficial burn. The biopsy shows a striking necrolysis of the cells of the upper epidermis and one comes to conceptualize that this is a *Necrolytic Migratory Erythema.* Awareness of an associated smooth shiny vermillion tongue, and the presence of hyperglycemia, allows one to direct the surgeon to the exact tumor site with recognition of even the cell line involved. Cure can be confidently expected if surgical intervention precedes metastasis.

With this we complete our scan of the signs and symptoms of the skin which alert both the patient and the physician to search for malignancy. Some are dramatic, bizarre and puzzling. Others are so commonplace as to suffer disregard. A few are disturbing and only that of the pancreatic tumors is distinctly unique. But every single one should stir us to *Think Cancer* in the great clinical tradition of Michelson.

Acknowledgment

My gratitude is expressed to Herman Beerman, M.D. for the privilege of access to his magnificent reprint collection on this subject. Photography was done by Edward F. Glifort.

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Tumors of the Skin

Premalignment and Malignant

PETER J. LYNCH, M.D.*

The most common premalignant and malignant tumors of the skin are discussed from a standpoint of characteristic features, differential diagnosis, and treatment.

MORBIDITY AND MORTALITY from malignant tumors of the skin should be totally preventable. Current therapeutic modalities would put this goal within reach if skin tumors could be accurately identified while still small. Ordinarily it is the patient's responsibility to bring early illness to the physician's attention; but skin cancer, like early cancer elsewhere, is essentially asymptomatic and often escapes the patient's attention. Family practitioners must therefore have sufficient interest and skill to recognize premalignant and malignant skin changes when they are examining patients for unrelated illnesses. On the other hand to avoid excessive cost and concern on the part of the patient, the family physician must recognize and dismiss the trivial skin lesions with which malignancy may be confused. In this presentation major emphasis will be placed on this "sorting" process through the discussion of characteristic clinical features and the differential diagnosis of lesions which look alike.

Premalignant Tumors

Actinic Damage and Actinic Keratoses

Characteristic Features. Actinically damaged skin occurs in a significant proportion of the American population. These changes are directly related to chronic sunlight exposure and they occur almost exclusively in patients with fair skin and light eye color. Actinic damage is confined to skin directly exposed to the sun, predominately the face, ears, and dorsal surface of the hands. Skin damaged by actinic exposure is recognized by the presence of hyperpigmentation, hypopigmentation and small telangiectatic vessels against a background of slight to moderate erythema (Figure 1). Actinic keratoses, which are localized areas of dysplastic epithelial cells, may occur against this general background. These keratotic lesions appear as superficial, poorly marginated, scaling papules with varying degrees of associated inflammatory erythema (Figure 1). Small keratoses are more easily palpated than visualized, but gray to light brown scale clearly marks the larger lesions. In some instances a small amount of serum may exude through the dysplastic epithelium giving the scale a yellow, crusted appearance. If left untreated, these keratoses eventually develop histologic evidence of squamous cell carcinoma.

Differential Diagnosis. Actinic keratoses are sometimes confused with seborrheic keratoses but the very sharp margin, lesser degree of scale formation, and soft brown color should help to identify the latter. Carcinomatous degeneration of actinic keratoses is recognized by the presence of palpable intra- or subcutaneous nodularity beneath the superficial scale formation.

Treatment. Because of their malignant potential, actinic keratoses require treatment. The dysplasia present in these lesions is confined to the epidermis, and thus treatment can be accomplished by superficial destruction. When the keratoses are few in number, they are most easily

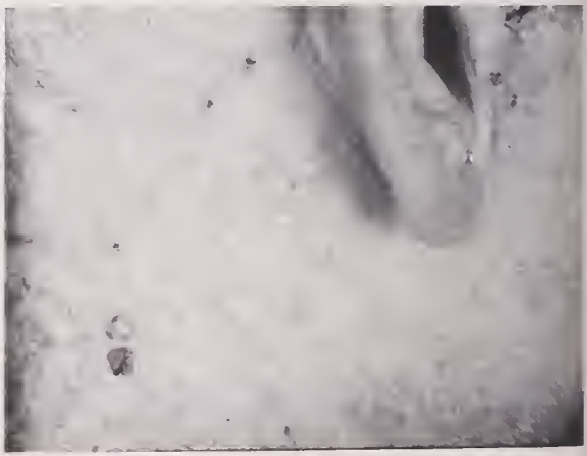

Fig. 1—Actinic damage with superimposed actinic keratoses.

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destroyed by the application of liquid nitrogen with a cotton tipped applicator. Light electrosurgery and the application of trichloracetic acid are also satisfactory but both result in greater discomfort and frequently lead to scarring. Excisional therapy is unnecessary and undesirable unless one is concerned about the presence of an underlying carcinoma.

When the actinic damage is widespread and the number of keratoses is large, topically applied 5-fluorouracil becomes the treatment of choice. This medication, originally developed for the treatment of systemic tumors, is available as a cream or solution in strengths of 1, 2, and 5%. The lower concentrations are used on the face and scalp while the 5% strength is used on the arms and hands. Either the cream or the solution is applied twice daily with the fingertips. Within several days of use, the treated skin becomes markedly inflammed. While the inflammatory reaction does not occur on normal, undamaged skin, both patients and physicians generally underestimate the extent of actinic damage and as a result are surprised by the amount of inflammation which develops. Patients need to be warned that this inflammation is an expected effect and not a manifestation of a drug reaction; they should, in fact, persist in treating the skin if the discomfort is not too severe. Treatment is generally carried out for three weeks by which time the inflammatory reaction has usually subsided spontaneously. A month or so after discontinuation of therapy the patient is re-examined and any remaining keratoses are destroyed with liquid nitrogen, electrosurgery, or trichloracetic acid. Patients are usually quite pleased with the eventual cosmetic improvement seen after 5-fluorouracil treatment and are generally willing to undergo retreatment whenever this proves necessary.

Actinic Chelitis

Characteristic Features. Chronic exposure of the lower lip to sunlight eventually results in actinic chelitis which is the mucosal equivalent of actinic keratoses. The two conditions have a somewhat similar appearance but in actinic chelitis, scale formation, as one might expect on a mucosal surface, is relatively slight. The earliest sign of actinic chelitis is the development of an irregular and indistinct vermillion border. Later the pink color of the mucosa becomes gray or white and the lip appears dry and chapped (Figure 2). No nodularity is present unless squamous cell carcinoma has developed in the area of actinic chelitis.

Differential Diagnosis. Leukoplakia represents more severe dysplasia and is characterized by the

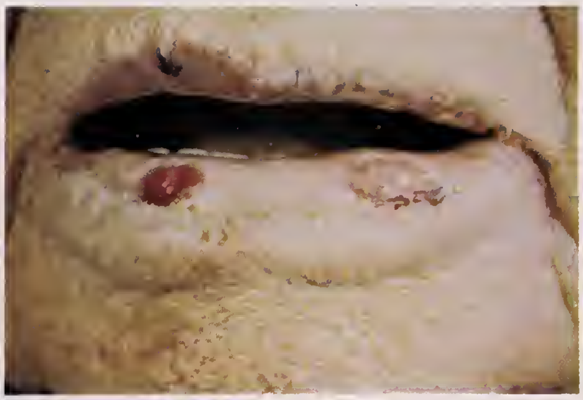

Fig. 2—Actinic chelitis with two areas of early squamous cell carcinoma.

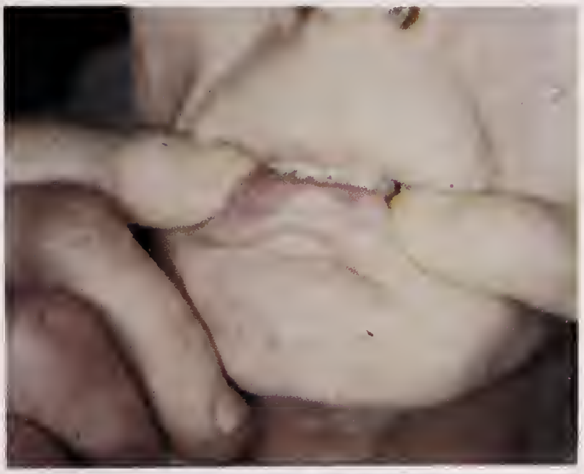

Fig. 3—Leukoplakia of the lip.

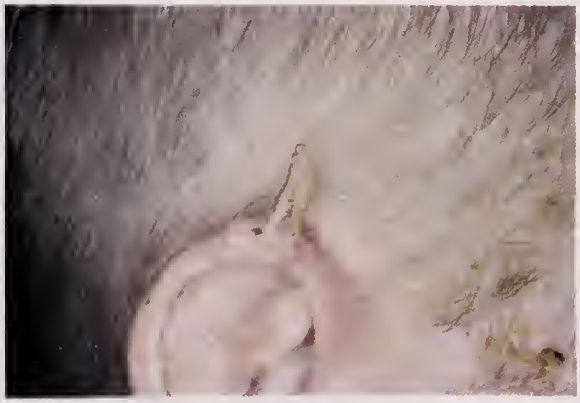

Fig. 4—Cutaneous horn with squamous cell carcinoma at the base.

presence of sharply marginated, soft, white plaques (Figure 3). The plaques are adherent to the underlying mucosa, a fact which helps separate leukoplakia from chronic candidiasis of the lip. Lichen planus of the lip results in a gray-white color change and thus may be confused with actinic chelitis but the pattern of color change is reticulated and the vermillion border remains intact.

Treatment. The application of liquid nitrogen as described above is suitable if the area of damage is small. Electrosurgery and trichloracetic acid also work well, and on the mucosal surface there is relatively little problem with scarring. 5-fluorouracil used as above, represents another satisfactory approach but when the dysplastic change is severe, there is good reason to consider wide excision with advancement of new mucosa from the inner lip.

Cutaneous Horn

Characteristic Features. A cutaneous horn is essentially a sharply marginated actinic keratosis with profuse and compact scale formation (Figure 4). As might be expected, most of these lesions occur on sun exposed skin.

Differential Diagnosis. On occasion it may be difficult to distinguish between a common wart and a cutaneous horn. However, the body of a wart is softer and the surface has multiple digitate projections. The presence of a palpable intra- or subcutaneous nodule at the base of a cutaneous horn should suggest the possibility of carcinomatous degeneration.

Treatment. The thick protective scale of the cutaneous horn makes the use of liquid nitrogen, trichloracetic acid ,and 5-fluorouracil more difficult and less effective. As a result, excision or deep shave biopsy followed by curettage and electrosurgery represent more appropriate approaches to therapy.

Lentigo Maligna

Characteristic Features. Lentigines are evenly pigmented, sharply marginated, brown macules which are larger and more permanent than freckles (Figure 5). They are generally located on sun exposed skin. The vast majority of lentigines have no malignant potential but occasionally those on the face will develop irregular speckling of dark brown or black pigmentation. The appearance of these color changes marks the development of the lentigo maligna (Figure 6), and biopsy of the dark speckled areas reveals atypical melanocytes at the dermal-epidermal junction. No proliferation or dermal invasion by these atypical melanocytes is present at this point, but with the passage of years these lesions do have the potential for eventual melanoma formation.

Differential Diagnosis. The lentigo maligna is clinically distinctive and there are no lesions with which it is likely to become confused. It may be difficult, however, to determine on a clinical basis whether or not actual melanoma formation has begun.

Treatment. Lentigines which lack the irregular pigmentation described above are benign and require no treatment. Whether or not treatment for the irregularly pigmented lentigo maligna is mandatory remains debatable. Certainly if any portion of the lentigo maligna has become papular, excisional biopsy of at least the elevated portion is absolutely necessary. Excision of non-papular lesions is probably desirable but may be technically difficult. Unfortunately, other means of destruction, such as with electrosurgery or trichloracetic acid, regularly result in recurrence. For this reason many clinicians prefer close observation as a reasonable alternative to elaborate or major excisional surgery.

Miscellaneous Premalignant Lesions

The giant hairy pigmented nevus is present at birth or develops during infancy. In perhaps 5% of these lesions, melanomas may develop. The likelihood of melanoma development is proportional to the surface area involved. If these pigmented nevi can be removed *in toto* without requiring too much reconstructive surgery, excision would seem desirable. For larger lesions, regular observation with excision of palpable nodules is a more practical approach.

The nevus sebaceous of Jadossohn also is present at birth or develops during infancy. In early life it is a slightly elevated, skin-colored plaque which usually occurs on the scalp or face. During puberty the plaque becomes more yellow in color and develops an irregular, pebble-like surface. Basal and squamous cell carcinomas eventually develop in a small proportion of these tumors and for this reason many clinicians recommend prophylactic excision and grafting.

Malignant Tumors

Nodular Basal Cell Carcinoma

Characteristic Features. The nodular basal cell carcinoma is the most common malignant tumor of the skin. It is a sharply marginated, skin colored nodule which has a waxy or translucent hue (Figure 7). Telangiectatic vessels may be seen on the surface of the nodule. The development of these tumors seems directly related to chronic sun exposure and thus they are almost exclusively found on exposed areas of persons with fair complexions and light eye color. The central area of the tumor becomes depressed as the lesion grows and eventually central ulceration develops (Figure 8). While these epitheliomas become locally invasive if left untreated, metastases, for all practical purposes, do not occur.

Differential Diagnosis. Hyperplastic or enlarged sebaceous glands may closely resemble small basal cell carcinomas. However, the former are yellow-white in color and have a minute depression representing the follicular orifice in the center of the lesion. The non-pigmented dermal nevus also resembles a basal cell carcinoma but the nevus is softer on palpation and lacks a waxy, translucent appearance.

Treatment. Prior to treatment a small fragment of tissue is removed for histologic examination. Then, using the dermal curet, the remaining soft, mushy tumor is scraped away. The base is treated with electrosurgery. Additional curettage followed by electrosurgery is repeated two or more times. Cure rates following this form of treatment are better than 95% and cosmetic acceptability of the hypopigmented, round scar is good. Excision also offers high cure rates and good cosmetic results and choice between the two procedures often depends on the skill of the operator. Radiation therapy, once widely used, is now preferred only for basal cell carcinomas occurring on the eyelids and in the naso-labial folds. Cryosurgery, in which liquid nitrogen is applied with a special probe or spray, has recently become quite popular but its eventual place in the treatment of these tumors has not yet been established. Moh's chemosurgery, which consists of frozen section examination of tissue fixed *in vivo,* offers exceptionally high cure rates; but limited availability and considerable expense restrict its use to very large tumors and those which have recurred following conventional therapy.

Pigmented Basal Cell Carcinoma

Characteristic Features. The relatively uncommon pigmented basal cell carcinoma warrants discussion because of its similarity to the superficial spreading melanoma (Figure 9). This tumor has all of the characteristics described for the nodular basal cell carcinoma but in addition has varying degrees of brown or gray-brown pigmentation and is more frequently found on the trunk than on the face.

Differential Diagnosis. The rather similar superficial spreading melanoma possesses a greater variety of colors, is less translucent in appearance, and is more likely to be lobulated or irregular in outline. Seborrheic keratoses, which are benign proliferations of relatively undifferentiated epidermal cells, also cause pigmented nodules on the trunk, face, and arms (Figure 10). However, the superficial appearance, which has often been likened to a drop of dirty candle wax, generally allows for correct identification.

Treatment. It is frequently necessary to excise a suspected pigmented basal cell carcinoma in order to rule out the presence of superficial spreading melanoma. If, however, the two can be differentiated with certainty, then incisional biopsy followed by curettage and electrosurgery is appropriate.

Superficial Basal Cell Carcinoma

Characteristic Features. Superficial basal cell carcinomas are sharply marginated, erythematous plaques several centimeters or more in diameter (Figure 11). They are most often found on the trunk and proximal extremities. Relatively little scale overlies the plaque and the flat exposed surface is surprisingly lacking in nodularity. Patients rarely suspect the true nature of these uncommon tumors because the plaques grow so slowly. Some patients with superficial basal cell carcinomas will have had arsenic exposure or superficial radiation therapy years prior to the development of the tumors.

Differential Diagnosis. These superficial tumors bear a striking resemblance to the individual plaques of localized neurodermatitis, nummular eczema, or psoriasis. Itching, lichenification, heavy scale formation, and a transient nature are more typical for these latter, benign diseases. Clinically it may be difficult to distinguish between superficial basal cell carcinoma and Bowen's disease (see below), but this is not of great

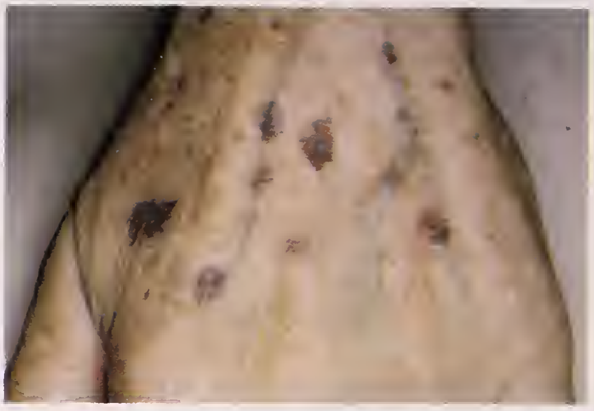

Fig. 5—Benign lentigines.

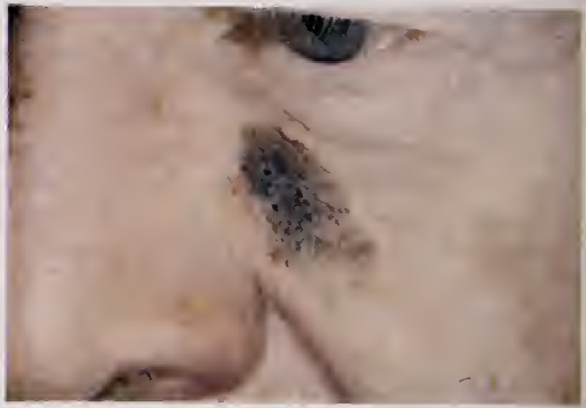

Fig. 6—Lentigo maligna of the face.

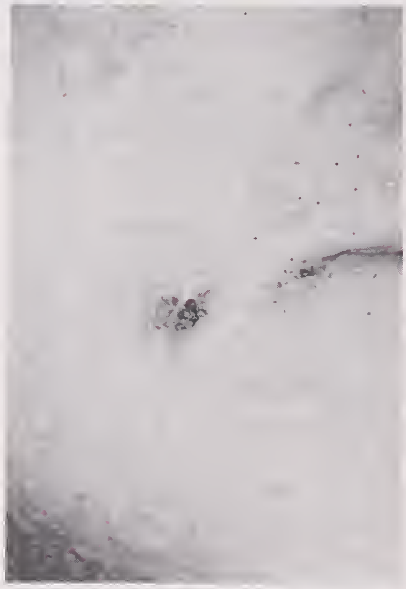

Fig. 7—Nodular basal cell carcinoma.

Fig. 8—Nodular basal cell carcinoma with central ulceration.

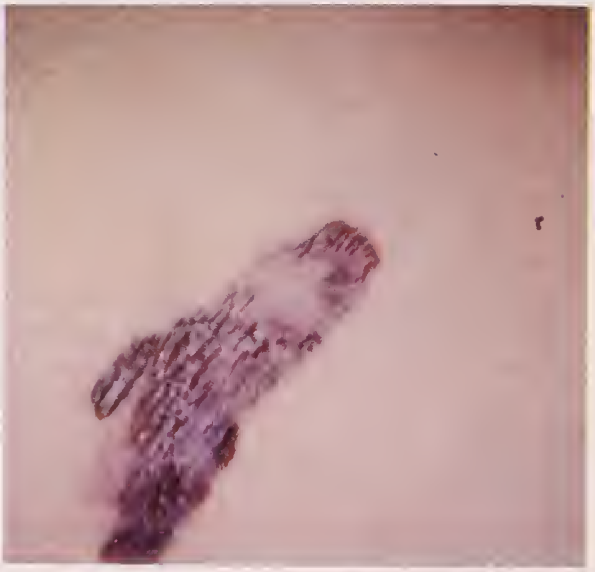

Fig. 9—Superficial spreading melanoma.

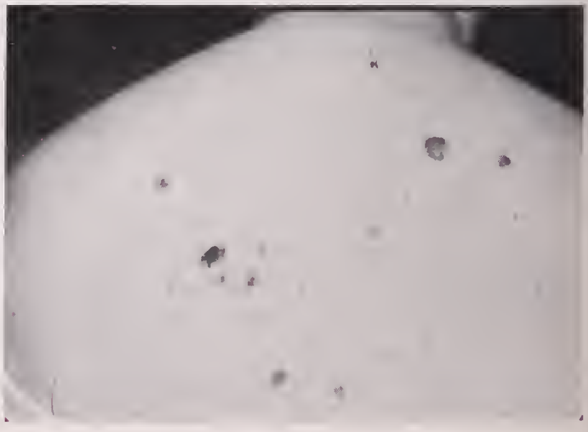

Fig. 10—Seborrheic keratoses.

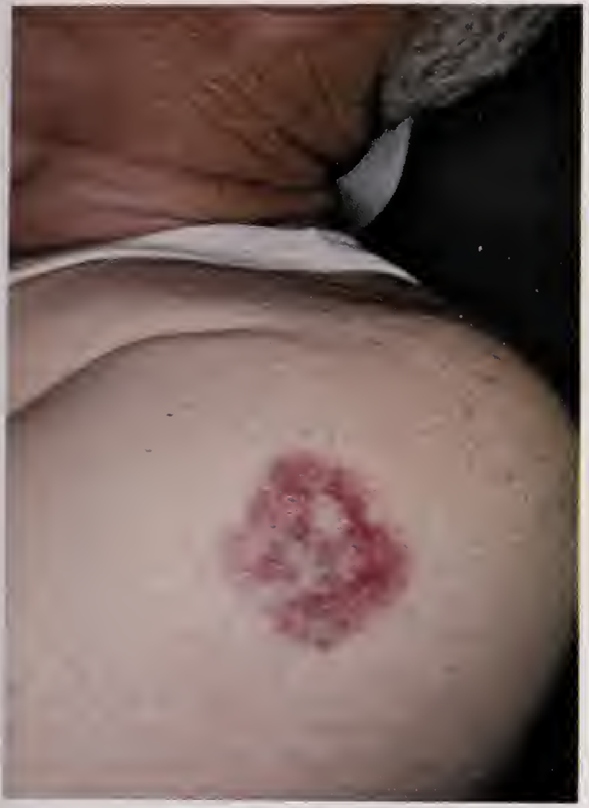

Fig. 11—Superficial basal cell carcinoma.

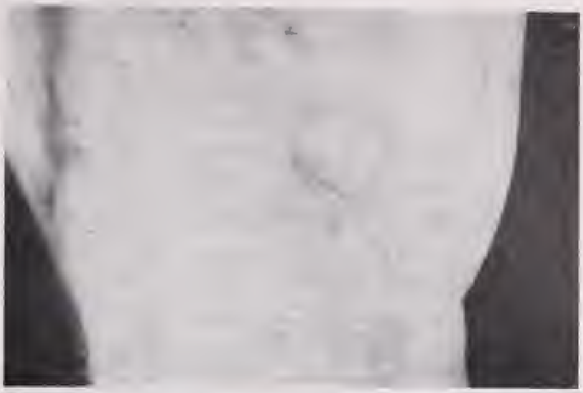

Fig. 12—Nodular squamous cell carcinoma.

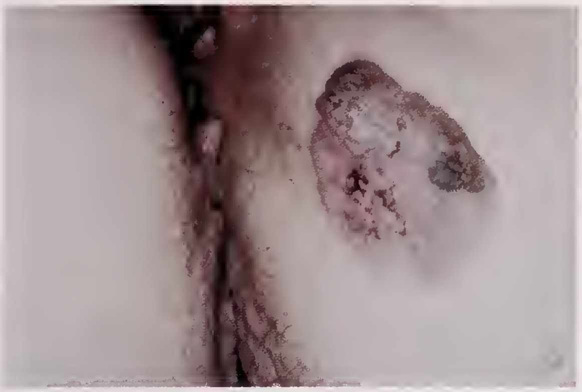

Fig. 13—Bowen's disease.

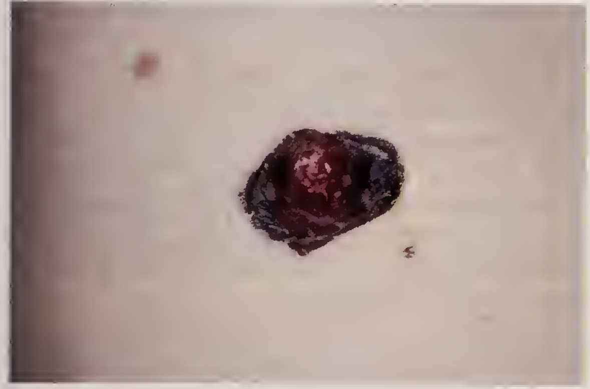

Fig. 14—Nodular melanoma.

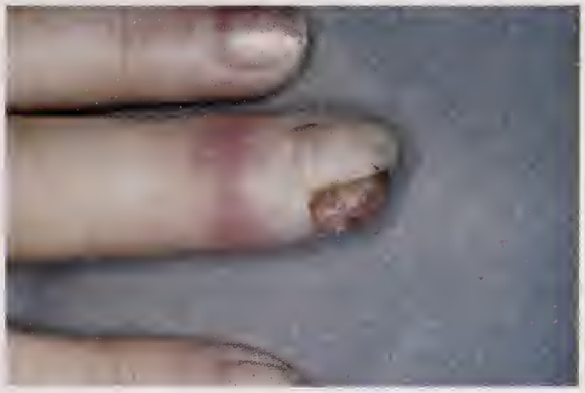

Fig. 15—Pyogenic granuloma.

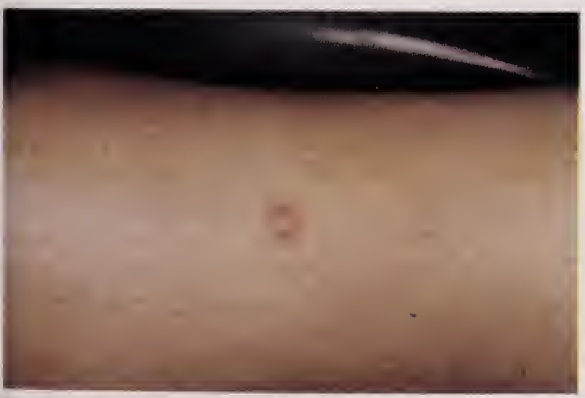

Fig. 16—Dermatofibroma.

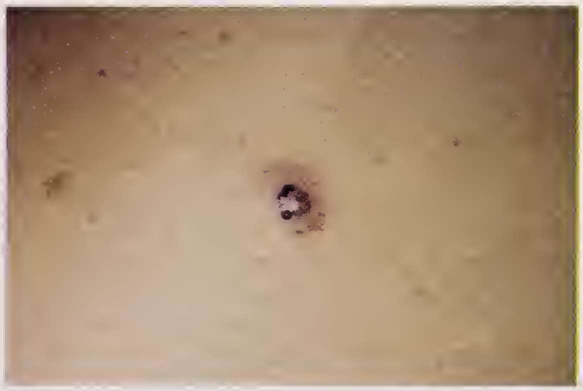

Fig. 17—Isolated angiokeratoma.

concern as the clinical course and treatment is similar for the two diseases.

Treatment. Curettage followed by electrosurgery is the treatment of choice for superficial basal cell carcinoma but cryosurgery is also useful. Radiation and excisional surgery are less acceptable because of the large surface area involved.

Actinic Squamous Cell Carcinoma

Characteristic Features. With the passage of time, actinic keratoses will develop histologic features of low grade squamous cell carcinomas. Often it is not clinically possible to tell when an actinic keratosis has turned the corner and become a squamous cell carcinoma. The best clinical clue is the development of an infiltrated base beneath the scale of an otherwise typical actinic keratosis. Squamous cell carcinoma appearing in these circumstances behaves in a relatively nonaggressive fashion; growth occurs slowly and metastases are rarely seen.

Differential Diagnosis. It may be difficult to distinguish basal cell carcinomas arising on actinically damaged skin from actinic squamous cell carcinoma. The latter is more likely to have overlying scale and is less likely to have a translucent, rolled border.

Treatment. Curettage followed by electrosurgery, as described for basal cell carcinomas, results in 95% cure rates. Excision is an acceptable form of therapy but poor visual definition of the borders makes placement of the surgical margins difficult. Radiation therapy and cryosurgery as described for basal cell carcinoma may be used in some instances.

Nodular Squamous Cell Carcinoma

Characteristic Features. The nodular squamous cell carcinoma is not necessarily preceded by actinic damage. It occurs as a skin colored, dome shaped, firm papule with little overlying scale (Figure 12). Central ulceration is seen in the larger lesions. The nodular squamous cell carcinoma is commonly seen on the lower lip and the dorsal surface of the hand but these lesions also arise in old scars and in the borders of chronic ulcers. The nodular squamous cell carcinoma behaves more aggressively than the actinic squamous cell carcinoma.

Differential Diagnosis. At times biopsy may be necessary to distinguish between nodular basal cell carcinoma and nodular squamous cell carcinoma. It is often impossible for most clinicians and most pathologists to positively distinguish between a keratoacanthoma (a generally benign tumor which grows quickly forming a central keratin plug) and a nodular squamous cell carcinoma. For this reason the two are usually treated in an identical manner.

Treatment. Excision is the treatment of choice for nodular squamous cell carcinoma as it allows histologic determination of the tumor margins. However, there is some evidence suggesting that radiation therapy and curettage followed by electrosurgery give equally good cure rates.

Bowen's Disease (In Situ Squamous Cell Carcinoma)

Characteristic Features. Bowen's disease is an eponym for squamous cell carcinoma *in situ*. The clinical appearance is that of a sharply marginated, slightly nodular, erythematous plaque (Figure 13). Usually only a single plaque is present and while it may be located anywhere, there is some predilection for the lower half of the body. Patients with Bowen's disease on skin unexposed to sun seem to have an increased incidence of internal cancer.

Differential Diagnosis. Biopsy is often necessary to distinguish Bowen's disease from superficial basal cell carcinoma and extra-mammary Paget's disease. It is probably unnecessary for the non-dermatologist to learn the distinguishing characteristics for these three uncommon diseases as long as he recognizes that they exist and have somewhat dissimilar implications.

Treatment. The treatment for Bowen's disease is the same as that for superficial basal cell carcinoma.

Lentigo Maligna Melanoma

Characteristic Features. As described above, melanoma may occur in a lentigo maligna. The developing melanoma occurs as a firm, black, poorly marginated papule arising from an irregularly pigmented patch. Histologically the nodule shows proliferation of atypical melanocytes with dermal invasion. Because these melanomas grow slowly, the prognosis following early removal is relatively good.

Differential Diagnosis. There are no lesions one is likely to confuse with the lentigo maligna melanoma, but it is sometimes difficult to determine clinically whether melanoma is or is not present in a lentigo maligna. When in doubt, excisional biopsy should be performed.

Treatment. Any elevated or palpable area occurring in a lentigo should be widely excised but the margins do not necessarily have to include all of the surrounding flat pigment. Histologic study of the excised tissue generally shows rather superficial melanoma formation and for this reason, regional lymphadenectomy is usually unnecessary.

Superficial Spreading Melanoma

Characteristic Features. The superficial spreading melanoma occurs as a flat topped nodule or plaque (Figure 9). Slow growth occurs in an uneven centrifugal manner resulting in a polycyclic or lobulated border; some healing may even be present in the center. Multiple colors, including browns, blacks, reds, and blues may be present in various parts of the lesion and are an important clue to the diagnosis. These melanomas grow rather slowly, and early removal results in a relatively good prognosis.

Differential Diagnosis. The pigmented basal cell carcinoma is the only lesion easily confused with the superficial spreading melanoma. The former lacks the rainbow hues and is less polycyclic in outline but when the lesions are small, excisional biopsy may be necessary to distinguish between the two diseases.

Treatment. Wide excision is the treatment of choice. If the histologic sections show only superficial invasion of the dermis, and if the lymph nodes are not enlarged, lymphadenectomy may not be necessary. If the lesion is large and a clinical diagnosis cannot be established with certainty, biopsy through the lesion is safe and acceptable.

Nodular Melanoma

Characteristic Features. The nodular melanoma is a firm, dome-shaped, brown or black nodule (Figure 14). Larger, older lesions may develop centrifugal spread of pigment and central ulceration. Unfortunately these melanomas grow quickly and behave in an aggressive fashion. As a result, metastases frequently occur before the tumor is recognized and excised.

Differential Diagnosis. Pyogenic granulomas may closely resemble nodular melanomas (Figure 15). These vascular tumors grow quickly and this together with their dark color often necessitates excisional biopsy. Seborrheic keratoses may also cause confusion but they are slowly growing lesions which have a superficial appearance and are flat topped rather than dome shaped. While a compound nevus can ordinarily be identified as a soft, pigmented papule which remains unchanged for many years, sometimes distinction between them and a melanoma is not clinically possible. The dermatofibroma is a firm, brown, intracutaneous nodule (Figure 16). It occurs most commonly on the legs. Occasionally during pregnancy, these darken and increase in size alarming both physician and patient. Finally, isolated angiokeratomas are uncommon dark blue or black vascular tumors which are regularly confused with melanomas (Figure 17).

Treatment. Wide excision of the nodular melanoma is the treatment of choice. Usually histologic examination reveals deep dermal invasion and for this reason regional lymphadenectomy is usually carried out regardless of whether or not the nodes are clinically enlarged.

Acne

Pathogenesis and Treatment

HERBERT MESCON, M.D.* AND STEVEN R. KOHN, M.D.†

A brief survey of the current concepts of pathogenesis and treatment of acne. The authors are still somewhat uncertain of the exact cause and do not yet have the cure. Those modalities that presently seem beneficial and their potential disadvantages are listed.

ACNE IS ONE of the commonest diseases of man. Although there is no mortality, it can cause discomfort, disfigurement and psychological stress. It is a disease of the pilosebaceous unit (PSU, hair follicle and oil glands) manifests by open and closed comedones, inflammatory papules, pustules, nodules and cysts which may eventuate in scarring (Figures 1-4). The incidence of acne in adolescents has been estimated at 50 to 60%;[1] a few comedones may be considered physiologic. Although acne usually occurs in adolescents, (the maximum incidence is between the ages of 15 to 20 years), it may occur in adulthood to middle life and may even be present in infants. The sebaceous glands in patients with acne are almost always well developed and usually produce an increased amount of sebum as compared to controls, although there is considerable overlapping. Many adolescents with oily skins do not develop acne. There appears to be an hereditary predisposition to acne but this has not been completely investigated and is not controllable at present.

Pathogenesis

The exact cause of acne is unknown, but much experimental work in the past 20 years has strongly suggested that it is a disease of the sebaceous gland and its associated follicle. In order to best utilize available therapy, an understanding of current concepts of pathogenesis is necessary. The pathogenic factors are interrelated and appear to be at least four: (A) problems of keratinization of the follicular epithelium, (B) the presence of follicular microflora, (C) the role of follicular lipids (sebum) produced by the sebaceous glands and (D) the role of hormonal control of sebaceous glands.

(A) *Keratinization* of the follicular epithelium is not well understood, but in acne a dense keratin plug containing bacteria and sebaceous lipids occurs. When the plugs are large, open comedones are seen clinically. At times the opening of the PSU is very narrow (not observed clinically) and only a small yellow papule is seen; this constitutes a closed comedone. This plug formation may be related to increased and/or abnormal proliferation and cohesiveness of the epithelial cells of the sebaceous follicles and its keratin.

(B) The *microflora* of the sebaceous follicle is composed of *Corynebacterium acnes,* staphylococci, and pityrosporum species. Acne must not be viewed as a bacterial disease "per se"; the disease appears to be in part a result of microorganisms' lipase activity which releases the irritating free fatty acids from the sebum.

(C) The amount of *sebum* produced by patients with acne is generally, but not always, above normal. Sebum contains several lipids. The free fatty acid portion is the most irritating and when injected experimentally into the skin, produces a reaction similar to that seen in inflammatory acne.[2] Sebum and its fatty acids have

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also been shown to form comedones when applied to the inner surface of the rabbit ear.[3] The earliest inflammatory lesion seems to result from penetration of the irritating fatty acids through the follicle wall into the adjacent dermis. As this increases there is marked erythema and inflammation and some foreign body reaction due to keratin released into the dermis. If severe enough,

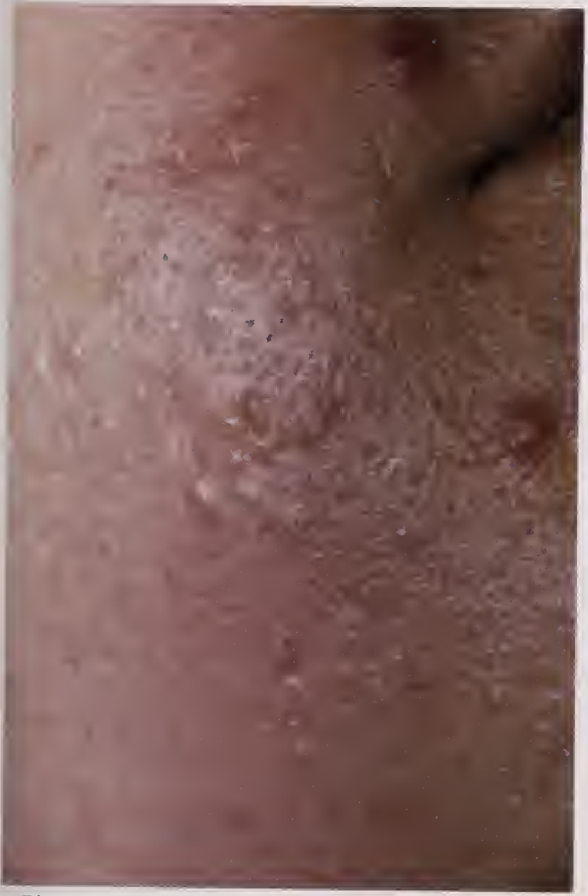

Fig. 1—Acne vulgaris: open and closed comedones, inflammatory papule and small pit-like scars.

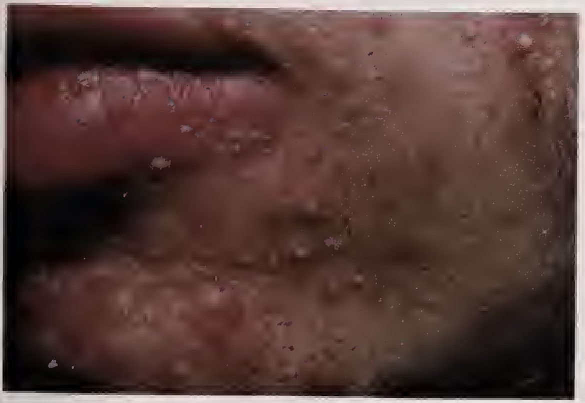

Fig. 2—Acne vulgaris: pustules and nodules.

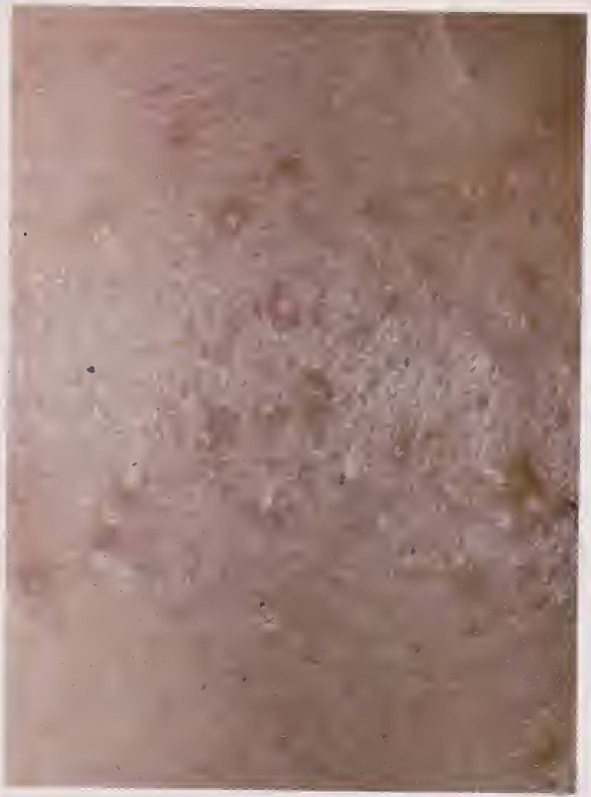

Fig. 3—Acne vulgaris: open and closed comedones, cysts and small pit-like scars.

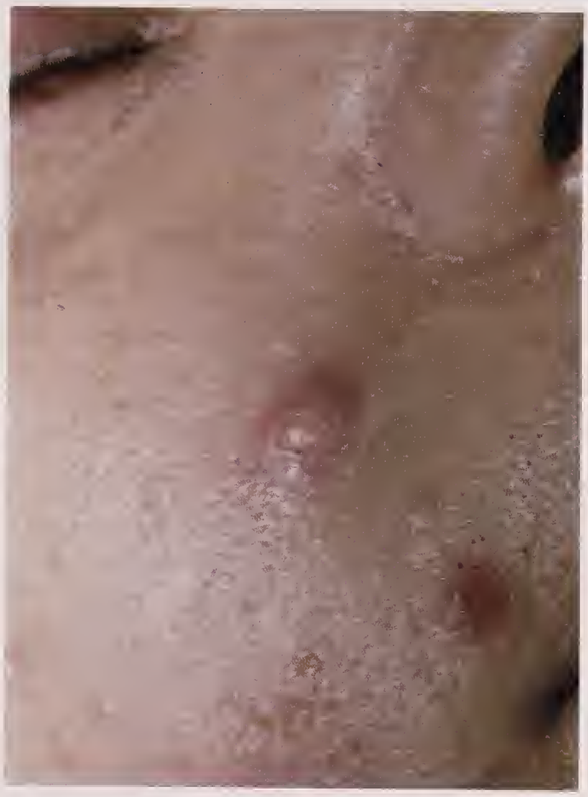

Fig. 4—Acne vulgaris: large inflammatory papule, closed comedones and small pit-like scars.

pustules, cyst formation and scarring may result. When sebum (free fatty acids) is reduced the acne generally improves. This will be discussed below.

(D) The pathogenic role of *hormonal control* of sebaceous glands is based on sebaceous glands being androgen dependent. Their size can be increased in prepubertals and castrated males by giving testosterone. Estrogens cause decrease in size of the glands but seem to act by inhibiting androgen production in both males and females. Locally, estrogens applied to the skin do not seem to be effective unless enough is absorbed to act systemically which may produce undesirable feminizing effects in the male, i.e., loss of libido, gynecomastia and voice alteration. Endocrine diseases where androgens from gonads or adrenals are produced in abnormally high amounts tend to cause increased sebum production and may result in acne. Systemic corticosteroids also increase the size and output of the sebaceous glands and produce steroid acne.

Therapy[4-7]

It must be kept in mind that the course of acne varies from patient to patient and even for a given patient. It is therefore difficult to evaluate precisely the benefits of any type of treatment. Based on the pathogenic concepts mentioned above, the following rational modalities may be used:

Acne Surgery

The mechanical removal of open comedones (blackheads) and closed comedones (whiteheads) (Figures 1, 3 and 4) is a relatively simple and effective procedure. A comedo extractor (a scoop or loop with a small central hole) can be used to remove blackheads by placing the extractor hole over the plug and exerting pressure against the skin. The blackhead will then be extruded through the hole in the extractor. A similar procedure may be used to remove whiteheads but the lesions usually must first be gently opened by a sterile needle, scalpel blade or the pointed end of the comedo extractor before pressure is applied. Acne surgery appears not only to give rapid improvement in the patient's appearance, but may also improve the course of the disease.

Drying-Peeling Agents

Because of the presence of keratin plugging in many acne lesions, therapeutic agents are used which reduce this and hopefully eliminate comedones. The agents tend to cause drying, peeling and erythema. The stronger, usually more effective agents, are also more irritating.

Chemical Agents

Commonly used agents range from degreasers and cleansers (routine and medicated soap, Sebanil, etc.), to abrasives (Brasivol Scrub Cleanser), to keratolytic chemicals, [salicylic acid, resorcinol and/or benzoyl peroxide (Transact, Benoxyl Lotion, Vanoxide Lotion)]. Some are flesh colored to act as a coverup (Liquimat, Sulfacet, Resulin Lotion, etc.). Some have light and dark shaded preparations to suit the patient's complexion.

Vitamin A acid (retinoic acid) has been reported to be an effective agent for comedone removal.[8] It may potentiate the beneficial effects of tetracycline in acne therapy. It seems to be among the more effective but also more irritating local agents. Therefore, patients must be cautioned to reduce frequency of use if too much irritation occurs. Concurrent use of retinoic acid and sun or sunlamps is inadvisable because of occasional marked irritation or burn reactions when these agents are used together.

Physical Agents

(a) Ultraviolet Light: Many patients with acne improve in the summer. The exact mechanism for this is unknown. Improvement may be due as much to psychological factors as to the erythema and desquamation from sun exposure. For these patients ultraviolet light seems to be a valuable therapeutic modality. Although natural sunshine is probably the best source of ultraviolet light, such exposure may not be possible. An artificial ultraviolet light source may be used. The inexpensive ones, i.e., screw-in ultraviolet bulb, are satisfactory for many patients. Usually a dose sufficient to cause at least some erythema is necessary. Obviously, the dose must vary with the degree of pigmentation of the patient. It is advisable to explain carefully the proper home use of ultraviolet light therapy. Because the dose varies inversely with the square of the distance from the lamp to the skin, the distance must be kept the same for each exposure. Only the time will be varied. The patient should start with a short time and increase each day until a mild burn occurs. Then one to two treatments per week are usually satisfactory. The time of exposure will have to be increased periodically to obtain a mild burn. Most dermatologists do not feel that a suberythema dose is of value. The eyes must be shielded by sunglasses or other opaque material. It is advisable to have an alarm timer and ideally another person in the vicinity to double check that the patient has not fallen asleep istries monitoring liver and renal function.

Patients often ask about the danger of skin cancer developing from ultraviolet treatment for acne. Long continued daily exposure over many years, e.g., farmers and sailors, can cause skin cancer. However, limited weekly or twice weekly exposure for a few months to several years has not been shown to be harmful. Naturally, patients who have a history of adverse reactions should not be treated with ultraviolet light.

(b) Cryotherapy: Pieces of dry ice alone or dry ice-sulfur-acetone slush have also been used as a drying-peeling agent.

(c) Antibiotics: Whereas acne surgery and the drying-peeling agents are effective in managing less inflammatory forms of acne, specifically blackheads and whiteheads, broad spectrum antibiotics, especially the tetracyclines, are usually effective in the treatment of inflammatory papules, pustules, nodules and cysts[9] (Figures 2 and 4). Systemic antibiotics should be administered *only* to patients who do not respond to milder, topical forms of therapy described above. A typical tetracycline regimen consists of 250 mg. p.o. b.i.d. for three weeks or longer until a positive result is obtained, followed by gradual reduction to the lowest dose sufficient to maintain control. Further cuts or cessation of therapy must be attempted periodically. It may be necessary at times, to return to higher dosage temporarily, but overall this is the only way to use the smallest necessary maintenance level. Because the sebaceous gland appears to act as an excretory route for tetracycline, this maintenance may be as low as 250 mg. p.o. q.o.d. Tetracycline should be taken on an empty stomach, e.g., one-half hour or more before meals or one to two hours after meals.

Although these low levels of tetracycline, even in long-term therapy, are relatively free from toxicity, an awareness of possible side effects is mandatory. This includes discoloration of deciduous and permanent teeth from the fourth fetal month through the twelfth year of life—therefore, tetracycline is not used in pregnant women or in children; possible liver damage, especially in the presence of renal disease; anaphylactoid reactions; nausea; diarrhea; and yeast superinfections. Some authorities advocate a laboratory checkup at the end of each six months of continuous or 12 months of intermittent, tetracycline therapy. This should include white blood count, hemoglobin, routine urine exam and some blood chemistries, monitoring liver and renal function.

In tetracycline-resistant patients, erythromycin and clindamycin may be effective, but must, of course, be used judiciously.

(d) Corticosteroids: Intralesional injection of corticosteroids such as hydrocortisone acetate or triamcinolone acetonide or acetate in appropriate concentration (0.05-0.20 ml of 10 mg/ml) is known to be an effective means of improving inflammatory papules, nodules and cysts, as well as reducing scarring. Occasional reversible atrophy may occur which is the reason for using small amounts in low concentrations as above. Topical steroids seem to be ineffective in acne.

Systemic corticosteroids are reserved for use only in rare cases of severe flaring of nodulocystic acne, because of their hazardous side effects and their ability to produce acne lesions themselves.

(e) Cyclic Estrogen-Progestin Therapy: The use of cyclic estrogen-progestin therapy ("oral contraceptives") in selected female patients is based on the possible role of hormonal control in the pathogenesis of acne.[10] As mentioned above, estrogens suppress sebum formation, probably by inhibiting androgen production. Because of the possibility of increased thromboembolic phenomena, as well as a multiplicity of other side effects, including premature cessation of bone growth, nausea, weight gain, spotting, breast tenderness, amenorrhea and chloasma, such hormonal therapy must be used with caution. Oral contraceptives should be administered in conjunction with gynecologic consultation and should

never be used before age 16 years, when maximum bone growth is obtained.

These agents are administered cyclically for three-week periods. Treatment is begun on the fifth day of menses and continued daily for 20 to 21 days. Following discontinuation of medication, bleeding ensues within a few days, and medication is renewed on day five as in the previous cycle. If withdrawal bleeding has not occurred by the seventh interval day, the medication is then restarted. The agents used for adequate sebaceous gland suppression should contain up to 0.1 mg of the estrogen, ethinyl estradiol, or its 3-methyl ether derivative, mestranol. In general, the effectiveness of this therapy parallels the amount of estrogens present in the medication. The amount of progestins in these medications does not seem to be important in acne therapy.

It may take three to four cycles for clinical improvement. If the lower dose estrogens (50 μmg) are ineffective, then the higher dose (80 μmg) should be used. In an occasional patient, the acne will flare early in the course of treatment, especially if the progestin has androgenic activity, e.g., norgestrel.

(f) Diet: Dietary management appears to be of little value in the treatment of acne. Occasionally a patient will have his disease aggravated by the ingestion of certain foods, especially chocolate. There is no scientific evidence that any group or type of food is particularly harmful, and most patients will tolerate all foods without ill effect on their acne. If a patient feels certain that a given food aggravates his acne, then advise him not to eat it.

(g) The role of tension in acne is unproven. Because of uncertainty about the natural course of this disease, and the difficulty of adequately measuring psychologic stress, it has been impossible to correlate tension and acne on a controlled basis. There is some experimental basis for correlating stress with adrenal cortical production, and this could indirectly cause acne. However, this last step has not been proven satisfactorily on a clinical basis. Although most physicians and many patients feel that such a correlation exists.

If the physician feels there is a relationship between acne and stress, then this should be presented to the patient, especially adolescents, with the explanation and reassurance that stress is to a large extent normal at that age. There are many readjustments and conflicts in the teenager (social, political, family adjustments, sexual, economic, educational, etc.). Fortunately, many of these problems are more easily handled by the patient as he matures. In many cases, reassurance alone can help patients cope with their acne.

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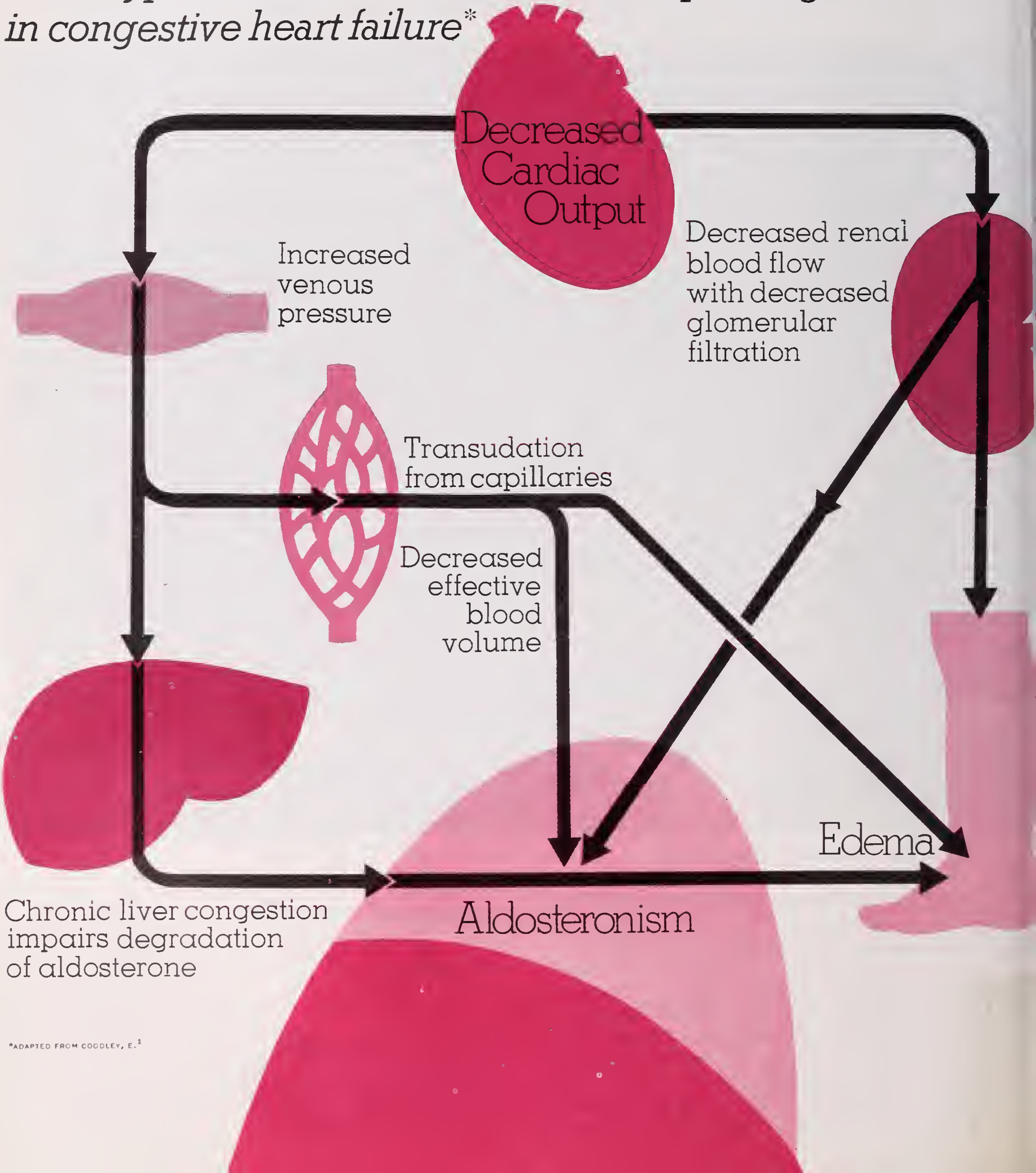
In congestive heart failure...
secondary aldosteronism

*How hyperaldosteronism leads to and prolongs edema in congestive heart failure**


Decreased Cardiac Output
Increased venous pressure
Decreased renal blood flow with decreased glomerular filtration
Transudation from capillaries
Decreased effective blood volume
Edema
Chronic liver congestion impairs degradation of aldosterone
Aldosteronism

*ADAPTED FROM GOODLEY, E.[1]

s a primary factor

o "switch off" the aldosterone factor in
ongestive heart failure

Aldactone

pironolactone 25-mg. tablets

he only specific
ldosterone antagonist…
asic in all diuretic therapy

hree ways to use Aldactone in
ngestive heart failure

As the only diuretic
Often sufficient alone.
Produces gradual, sustained diuresis by
ocking aldosterone action in the distal
nal tubule.
Avoids potassium loss.

As the basic daily diuretic with an "add-on"
ternate-day-diuretic ("A.D.D." schedule)
Can be administered daily as basic
erapy with the additional agent
rosemide or ethacrynic acid) given
ery second or third day.
Aldactone plus "A.D.D." schedule
inimizes potassium deficiency and
tentiates effect of "add-on" diuretic.[2]
Avoids acute volume depletion and
dosterone rebound.[2]

As a daily diuretic in combination with
daily dose of a thiazide
Permits daily additive diuretic effect
hile maintaining potassium balance.

Indications—Essential hypertension; edema or ascites of congestive heart failure, cirrhosis of the liver and the nephrotic syndrome; idiopathic edema. Some patients with malignant effusions may benefit from Aldactone (spironolactone), particularly when given with a thiazide diuretic.

Contraindications—Acute renal insufficiency, rapidly progressing impairment of renal function, anuria and hyperkalemia.

Warnings—Potassium supplementation may cause hyperkalemia and is not indicated unless a glucocorticoid is also given. Discontinue potassium supplementation if hyperkalemia develops. **Usage of any drug in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the mother and fetus.**

Precautions—Patients should be checked carefully since electrolyte imbalance may occur. Although usually insignificant, hyperkalemia may be serious when renal impairment exists; deaths have occurred. Hyponatremia, manifested by dryness of the mouth, thirst, lethargy and drowsiness, together with a low serum sodium may be caused or aggravated, especially when Aldactone is combined with other diuretics. Elevation of BUN may occur, especially when pretreatment hyperazotemia exists. Mild acidosis may occur. Reduce the dosage of other antihypertensive drugs, particularly the ganglionic blocking agents, by at least 50 percent when adding Aldactone since it may potentiate their action.

Adverse Reactions—Drowsiness, lethargy, headache, diarrhea and other gastrointestinal symptoms, maculopapular or erythematous cutaneous eruptions, urticaria, mental confusion, drug fever, ataxia, gynecomastia, inability to achieve or maintain erection, mild androgenic effects, including hirsutism, irregular menses and deepening voice. Adverse reactions are infrequent and usually reversible.

Dosage and Administration—For **essential hypertension** in **adults** the daily dosage is 50 to 100 mg. in divided doses. Aldactone may be combined with a thiazide diuretic if necessary. Continue treatment for two weeks or longer since an adequate response may not occur sooner. Adjust subsequent dosage according to response of patient.

For edema, ascites or **effusions** in **adults** initial daily dosage is 100 mg. in divided doses. Continue medication for at least five days to determine diuretic response, add a thiazide or organic mercurial if adequate diuretic response has not occurred. Aldactone dosage should not be changed when other therapy is added. A daily dosage of Aldactone considerably greater than 75 mg. may be given if necessary.

A glucocorticoid, such as 15 to 20 mg. of prednisone daily, may be desirable for patients with extremely resistant edema which does not respond adequately to Aldactone and a conventional diuretic. Observe the usual precautions applicable to glucocorticoid therapy; supplemental potassium will usually be necessary. Such patients frequently have an associated hyponatremia—restriction of fluid intake to 1 liter per day or administration of mannitol or urea may be necessary (these measures are contraindicated in patients with uremia or severely impaired renal function). Mannitol is contraindicated in patients with congestive heart failure, and urea is contraindicated with a history or signs of hepatic coma unless the patient is receiving antibiotics orally to "sterilize" the gastrointestinal tract.

Glucocorticoids should probably be given first to patients with nephrosis since Aldactone, although useful for diuresis, will not directly affect the basic pathologic process.

For **children** the daily dosage should provide 1.5 mg. of Aldactone per pound of body weight

References: 1. Coodley, E.: Consultant 12:106-107, 109, 111, 113, 115 (July) 1972 **2.** Thorn, G. W., and Lauler, D. P.: Am. J. Med 53:673-684 (Nov.) 1972.

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The Role of the Detail Man

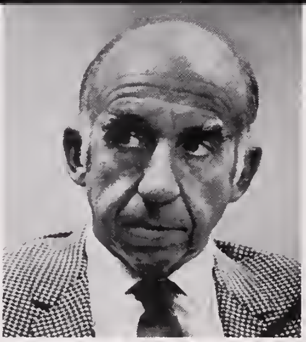
Opinion & Dialogue

Dr. Willard Gobbell
Family Physician
Encino, California

"I may be prejudiced, but I a
very much in favor of the detail m
I meet. Most of them are knowled
able about the drugs they promot
and can be a great help in acquair
ing me with new medication."

Family Physician's Perception

I think that most general
practitioners in this area feel as I
do about the detail man. Over the
years I have gotten to know most c
the men who visit me regularly an
they in turn have become aware o
my particular interests and the na
ture of my practice. They, there-
fore, limit their discussion as muc
as possible to the areas of interest
to me. Since I usually see the sam
representative again in future
visits, it is in his best interest to
supply me with the most honest,
factual, as well as up-to-date
information about his products.



Dr. Jeremiah Stamler
Chairman
Department of Community
Health and Preventive
Medicine, and Dingman
Professor of Cardiology
Northwestern University
Medical School

"In the total picture of dealin
with health problems in this count
there is a potential for detail men
to play a meaningful role."

The Positive Influence

My contact with representa-
tives and salesmen of the pharma-
ceutical industry is the type of con
tact that people in a medical cente
research people, and academic
people have and that's in all likelih
on a somewhat different level from
that of the practicing physician.

Let me touch on how I person
ally perceive the role of the sales
representative. These men reach
large numbers of health profes-
sionals. Thus they could be—and
at times actually are—dissemina-
tors of useful information. They
could consistently serve a real edu
cational function in their ability to
discuss their products.

At present they do distribute
printed material, brochures and
pamphlets—some of it scientific-
ally sound and therefore truly use-
ful—as well as some excellent film
produced by the pharmaceutical
industry. When they function in thi

He a Source of Information?

Yes, with certain reservations. he average sales representative as a great fund of information oout the drug products he is re- onsible for. He is usually able to iswer most questions fully and telligently. He can also supply prints of articles that contain a eat deal of information. Here, o, I exercise some caution. I usu- ly accept most of the statements d opinions that I find in the pers and studies which come om the larger teaching facilities. goes without saying that a physi- an should also rely on other urces for his information on armacology.

aining of Sales Representatives

Ideally, a candidate for the sition as a sales representative a pharmaceutical company ould be a graduate pharmacist no has a questioning mind. I don't ink this is possible in every case, d so it becomes the responsibility of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

---

pacity they are indeed useful; rticularly in the fact that they sseminate broadly based educa- nal material and serve not just "pushers" of their drugs.

e Other Side of the Coin

Obviously, the pharmaceuti- companies are not producing all s material as a labor of love— y are in the business of selling ducts for profit. In this regard ambitious and improperly moti- ed sales representative can rt a negative influence on the cticing physician, both by pre- ting a one-sided picture of his duct, and by encouraging the ctitioner to depend too heavily drugs for his total therapy. In se ways, the salesman has often torted objective reality and dermined his potential role as an icator.

Industry Responsibility

Since the detail man must be nformation resource as well as epresentative of his particular rmaceutical company, he uld be carefully selected and thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.,* the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that information must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005

P·M·A

A Primer of Collagen Disease

DENNY L. TUFFANELLI, M.D.*

The clinical features, laboratory findings and management of the three classic "collagen" diseases are discussed.

LUPUS ERYTHEMATOSUS, typically a disease of young women, is usually manifested by multisystem involvement. Remissions and exacerbations occur frequently. Common clinical manifestations include: arthritis, fever, lymphadenopathy, myalgia, pleurisy, pericarditis, central nervous system symptoms, leukopenia, and anemia.

Pathogenesis

The pathogenesis of lupus erythematosus is unknown. Genetic predisposition, certain drugs, sunlight, autoimmunity, circulating soluble antigen-antibody complexes, and viruses have all been suggested to play a role. A familial incidence of lupus erythematosus has been reported in over 50 families, and protein abnormalities in asymptomatic relatives have been repeatedly observed. We recently reported a family in which six members had lupus erythematosus and a seventh family member subsequently developed lupus erythematosus during pregnancy. We are aware of seven reports of lupus erythematosus in identical twins.[1-3]

Drugs have also been related to the onset of systemic lupus erythematosus (SLE) or an SLE like syndrome. In most cases it is uncertain whether the syndrome is drug-induced or whether the drug uncovers latent lupus erythematosus. When the inducing drug is withdrawn, the lupus erythematosus syndrome usually will resolve. Procainamide is the most frequent and most accepted of the systemic lupus erythematosus inducers. Procainamide lupus differs from the idiopathic disease in the low incidence of kidney and skin involvement, absence of antibody to DNA, and absence of decreased serum complement.[4] Other inducing drugs include hydralazine, sulfonamides, penicillin, trimethadione, diphenylhdantoin and phenylbutazone. Several authors have reported an association between the use of oral contraceptives and the exacerbation of rheumatic complaints, or the induction of ANA and LE cells.[5] It would seem wise to consider other types of contraception in patients who have lupus erythematosus before prescribing "the pill," particularly for the patient with a previous history of an exacerbation during pregnancy or with menses (Figure 1).

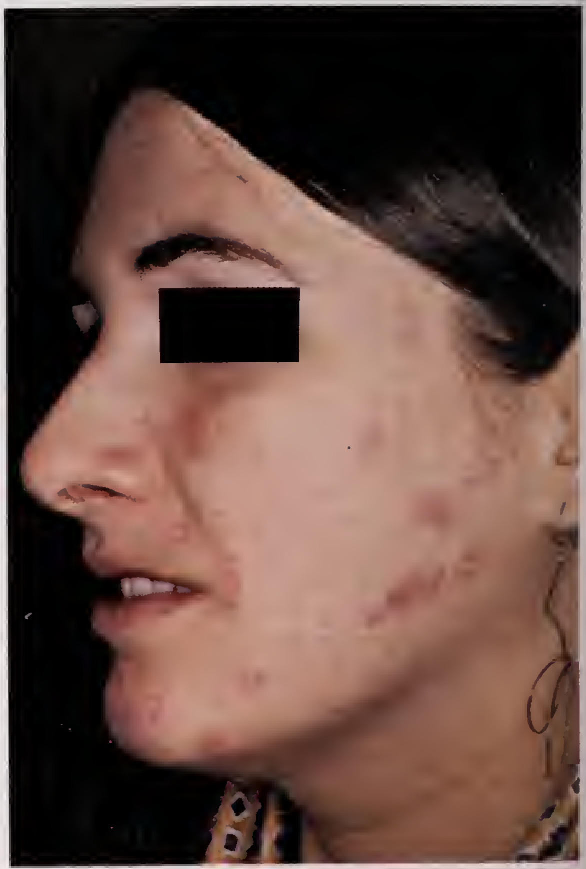

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Fig. 1—Twenty-seven year old female who developed cutaneous and serologic L.E. while taking birth control pills on two occasions and went into remission when off the pill.

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*Associate Clinical Professor of Dermatology, University of California, San Francisco, California.

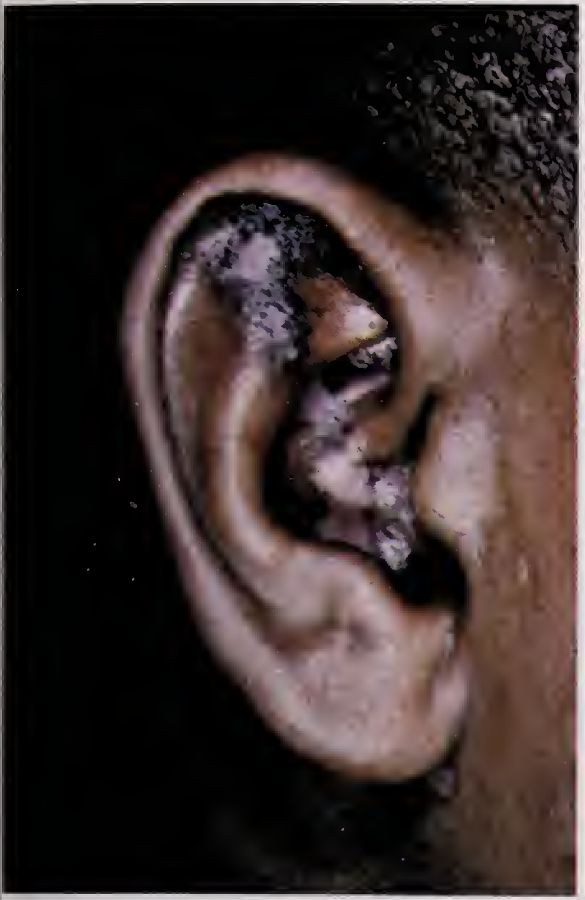

Fig. 2—Typical involvement of the ear in a patient with systemic lupus.

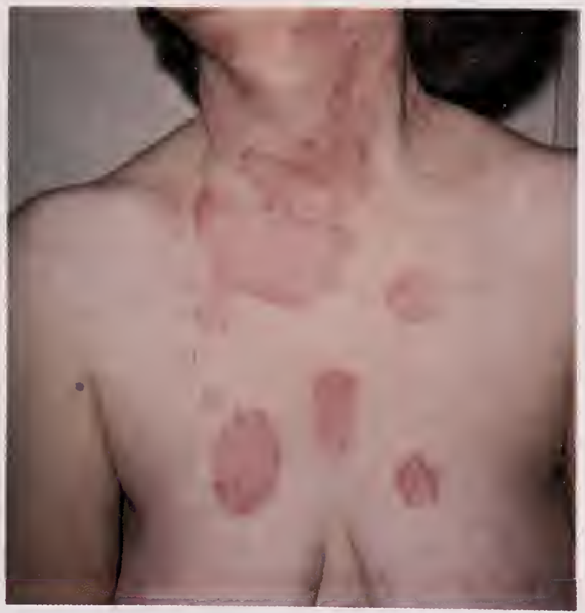

Fig. 3—Annular lesions of cutaneous lupus. These are quite unusual.

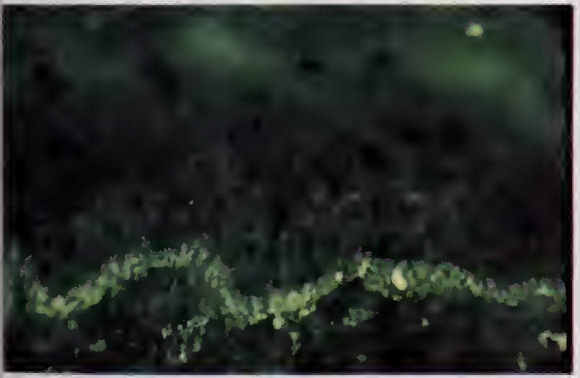

Fig. 4—Deposition of IgG at the dermal-epidermal unction in clinically normal skin in systemic lupus.

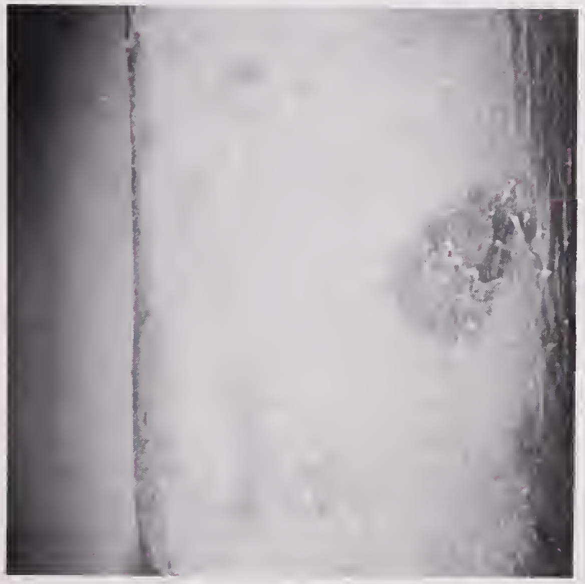

Fig. 5—Cutaneous atrophy and ecchymosis secondary to treatment of cutaneous lupus with a topical fluorinated corticosteroid cream.

Sunlight is a frequent predisposing factor, particularly for cutaneous lupus although severe systemic exacerbations can also follow sun exposure; release of altered DNA following actinic irradiation could possibly precipitate or exacerbate lupus erythematosus.

The implication of viruses as etiologic agents is suggested by the finding of virus-like cytoplasmic tubular structures in renal biopsies.[6] Such paramyxovirus-like structures have also been demonstrated in cutaneous lesions. Tubulo-reticular structures are also found in lymphocytes of patients with discoid and systemic LE.[7] They are not specific for lupus erythematosus, being found in other diseases.[8] Demonstration of significantly elevated antibody titers to several viruses has further stimulated interest in a possible viral pathogenesis.[9] A significant increase in antibodies to myxovirus, particularly measles, parainfluenza types 1 and 2, Epstein-Barr and rubella has been found in systemic lupus erythematosus.[10]

A wide variety of humoral and cellular antibodies has been demonstrated in lupus erythematosus. These include the following: lupus erythematosus factor, anticardiolipin, anticoagulants, leukocyte and red blood cell antibodies, rheumatoid factor, and antibodies to cellular constituents. Nuclear antigens and antibody include native (double-stranded) and denatured DNA, RNA, nucleoprotein, histone, a saline-soluble nuclear component (Sm), and extractable nuclear antigen (ENA). Cytoplasmic antigens include ribosomes and lysosomes.

There have been several studies of antibody response in systemic lupus erythematosus. There is no evidence of increased humoral antibody response to ordinary antigens.[11] Diminished antibody response to some antigens has been reported.[12] The status of delayed hypersensitivity in lupus erythematosus is not clear, though reports of hyporesponsiveness have appeared.[13]

Cutaneous Manifestations

Discoid lupus erythematosus is the chronic cutaneous form of lupus erythematosus. The reported incidence of cutaneous manifestations in systemic lupus erythematosus varies between 60 and 72 percent.[14] The detrimental effect of sunlight in lupus erythematosus is well known, although photosensitivity is not a consistent or essential part of the disease. The discoid form may transform into the systemic form. The recorded incidence varies from 2% to 20%, depending on the clinical group studied and the methods of analysis. Serological and hematological abnormalities are frequently noted in discoid lupus. It is the same disease as systemic lupus erythematosus but represents the more benign ranges of the lupus erythematosus spectrum.

Cutaneous lesions are characterized by erythema, adherent scales, follicular plugging, telan-

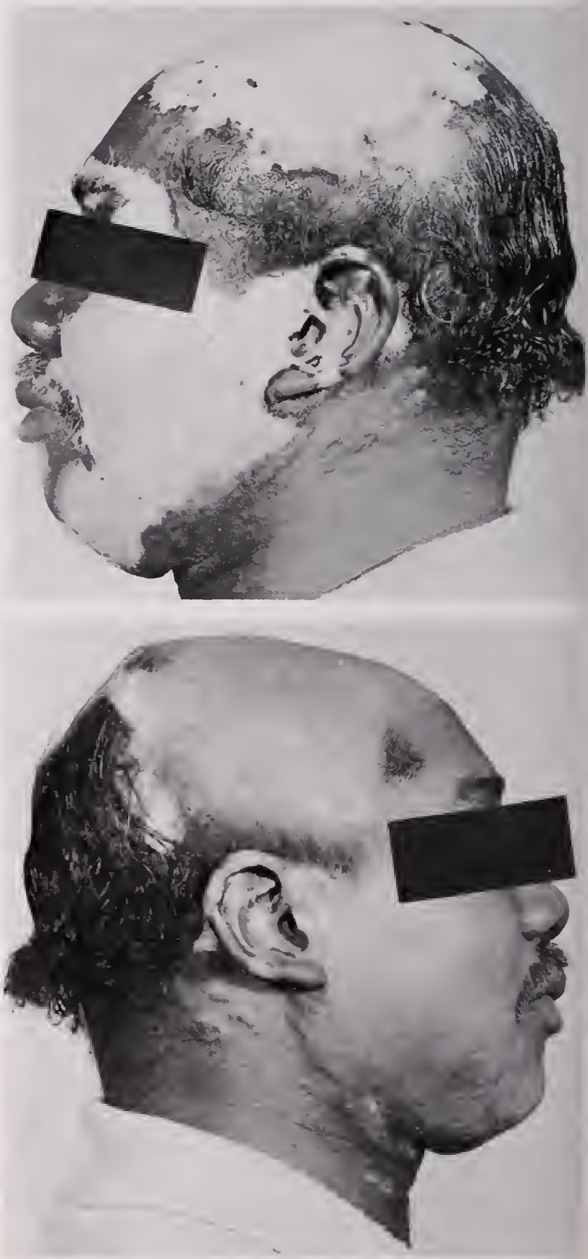

Fig. 6—This patient with cutaneous lupus has a most difficult cosmetic problem. The physician must recognize this, and spend time in counseling. The use of a covering agent was essential in the patient's management.

giectasia, and atrophy. Some lesions form permanent scars; others completely resolve. Hyperpigmentation and hypopigmentation often occur (Figures 2 and 3). Mucous membrane lesions occur especially during acute systemic episodes. Petechiae, purpura, and ecchymosis occur. Severe forms of vasculitis lead to the development of infarctive digital lesions, leg ulcers, and gangrene of the digits. Raynaud's phenomenon occurs in 20 percent of patients with systemic lupus erythematosus. Lupus erythematosus and porphyria cutanea tarda are occasionally associated.[15]

Systemic Manifestations

Fever is a common symptom and may persist without other symptoms or abnormal laboratory values. Persistent arthralgia, stiffness, and discomfort with no permanent changes in the joint are the common features. A characteristic of the arthritis of systemic lupus erythematosus is marked soft tissue swelling in the area of the involved joint. Gonococcal arthritis can occur in patients with systemic lupus erythematosus.[16] It is a curable cause of polyarthritis in systemic lupus erythematosus, and, because of the recent increased incidence, should be diagnostically considered, particularly when the polyarthritis is refractory to steroids.

Myalgias are commonly seen; muscle weakness due to lupus erythematosus myopathy is less often seen. Patients with vacuolar myopathy associated with systemic lupus erythematosus have been described.[17] Vacuolar myopathy has also been reported with steroid and chloroquine therapy.[18] Numerous cases of patients with systemic lupus erythematosus and avascular bone necrosis have been reported.

Lupus erythematosus heart disease can appear as pericarditis, myocarditis, cardiomegaly, nonspecific murmurs, ST segment changes and, later, heart failure.[19] Pericarditis has been estimated to occur clinically in 25% of cases.[20] Libman-Sachs verrucous endocarditis occurs rarely in lupus erythematosus.[21] This diagnosis can frequently be made only on postmortem examination. Pleurisy with or without effusion is probably the most common clinical pulmonary finding primarily related to lupus. True lupus pneumonitis is rare and is characterized roentgenographically by patchy, pulmonary infiltrates. It may represent a pulmonary vasculitis.

Esophageal involvement similar to that in scleroderma, with loss of peristalsis and dilatation of the esophagus and small intestine, may occur.[22] Jaundice has been noted in 3.8 percent of all age groups[14] and is usually due to either hemolytic anemia or hepatitis. It is not a usual feature of lupus erythematosus, although liver function tests may be abnormal, due to changes in serum proteins.

Central nervous system (CNS) disease is the second most frequent cause of death. The neurologic signs usually are mild and transitory. Central nervous system disease symptoms are present in 25% of patients, and peripheral neuritis present in 12%.[23] Convulsions, psychoses, and disturbances of mental function are common. The occurrence of convulsions and coma is frequently a sign of severe CNS involvement and is a grave prognostic sign. Many signs of psychiatric abnormalities occur, depending on the basic personality pattern. Psychoses in systemic lupus erythematosus may be secondary to steroid treatment, intrinsically related to active systemic lupus erythematosus, or represent psychiatric illness precipitated by the systemic lupus erythematosus.[24]

Renal disease is a common and ominous component of systemic lupus erythematosus. Clinically, the finding of more than six leukocytes or red blood cells per high-power field in a clear urine specimen is believed to indicate active kidney disease.[25] Proteinuria of over 1 gm/24 hr, red blood cell casts, oval fat bodies, and impaired renal function (blood urea nitrogen [BUN] or serum creatinine) indicate definite renal disease. The presence or absence of renal involvement can be proved only by biopsy, as test results of the urine can be negative in active disease. The nephrotic syndrome is common in children with renal lupus erythematosus. In general, patients with decreased renal function and lupus nephritis have a poor prognosis, although exceptions do occur.[26]

The presence of DNA, anti-DNA, and complement in the glomeruli from patients with lupus nephritis has been demonstrated. Sera from patients with active renal disease usually contain an outlined ANA pattern, high levels of anti-DNA antibodies, and low serum complement levels.[27]

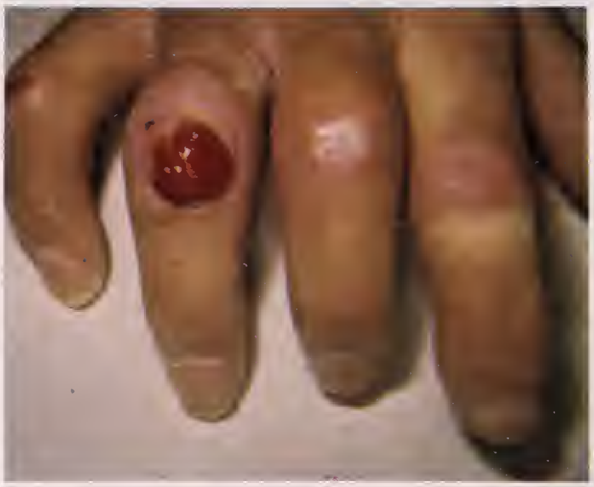

Fig. 7—A pyogenic granuloma has developed on the hand of this patient who otherwise has the typical features of scleroderma.

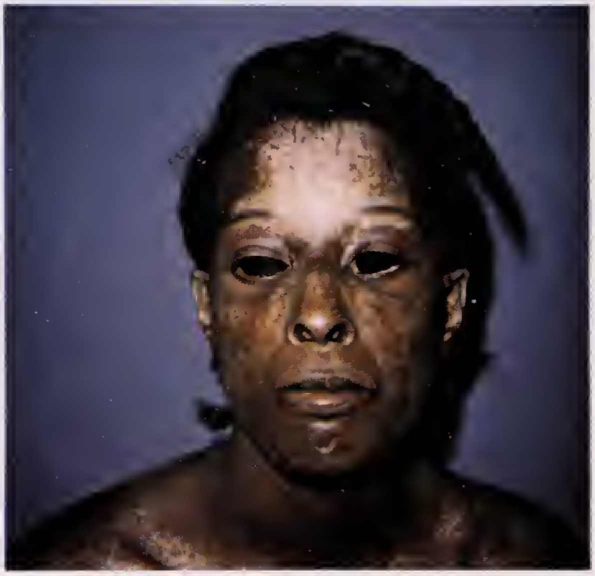

Fig. 9—This patient had typical systemic scleroderma. However, the cosmetic problem caused by depigmentation was her chief concern.

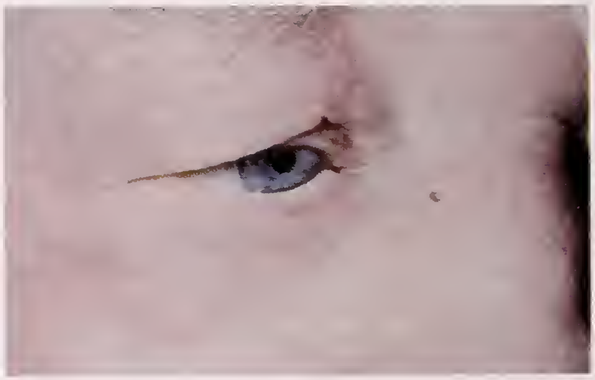

Fig. 11—The violaceous hue, particularly around the eyes, is essentially diagnostic in this patient with dermatomyositis, and a lung carcinoma.

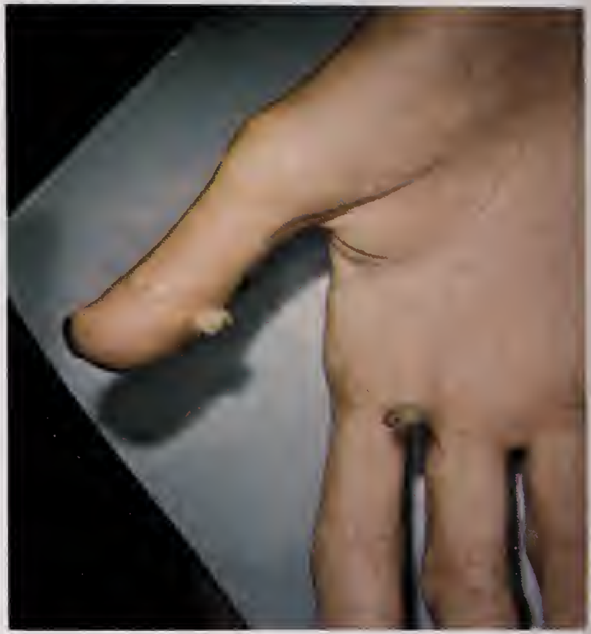

Fig. 8—Cutaneous calcinosis occurs in more than 10% of patients with scleroderma.

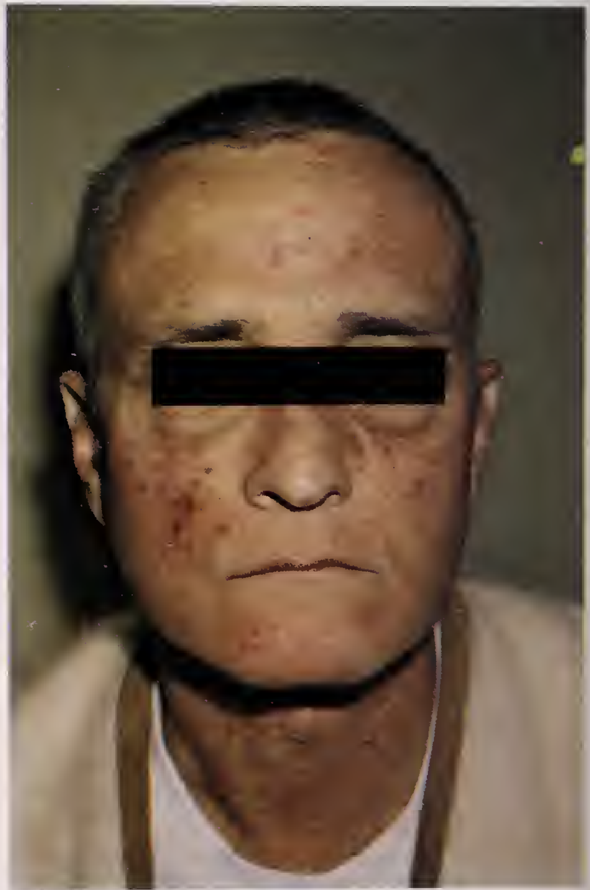

Fig. 10—Facial telangiectasia, as demonstrated in this patient, should always suggest the diagnosis of scleroderma.

Laboratory Findings

Laboratory work commonly demonstrates the presence of anemia, leukopenia, thrombocytopenia, or urinary tract abnormalities. The sedimentation rate is elevated in most patients. Abnormalities of plasma protein, particularly IgG elevation, are common but are not diagnostic. Rheumatoid factor may be positive. A major advance in the understanding of lupus erythematosus was the discovery of the lupus erythematosus cell in 1948.[28] It is the most specific test for lupus erythematosus.

The fluorescent antinuclear-antibody test involves identification of antibody gamma globulin on a cell nucleus.[29] A positive preparation will appear in various patterns: homogenous (diffuse), speckled, nucleolar, or outlined. The homogeneous type of staining is the most common. The antinuclear-antibody test is more sensitive but less specific than the lupus erythematosus cell test. Positive lupus erythematosus cell tests occur rarely, if at all, in patients with negative antinuclear-antibody tests. The latter is an excellent screening procedure.

Specific reactions with DNA and RNA may be helpful diagnostically. DNA antibodies in lupus erythematosus are currently receiving much interest. DNA antibodies are found in one third to two thirds of systemic lupus erythematosus sera tested[30] and are highly specific. Normal values are found in drug-induced lupus, discoid lupus, and lupoid hepatitis. There appears to be a correlation between DNA antibody titer and disease activity.[31]

Wassermann reagin is found in approximately 10 percent of patients with lupus erythematosus. In addition, patients with systemic lupus erythematosus may have an atypical false positive "beading" fluorescence pattern when the FTA-ABS test is performed.[32] Serum complement levels are often low in patients with active systemic lupus erythematosus, especially in the presence of lupus nephritis. As the activity of this disease increases, the serum complement usually decreases. Petz et al.[33] have reported that cerebrospinal fluid hemolytic C4 titers are a sensitive assay for CNS lupus erythematosus and not a reflection of serum values. Estimation of spinal fluid complement is of practical value in the management of patients with possible CNS lupus erythematosus.

Cutaneous Pathology

Study of cutaneous biopsy specimens by light, immunofluorescent, and ultrastructural microscopy is most useful diagnostically, and each should be used when indicated.

Early skin lesions may show only sparse and nonspecific changes. However, the following changes are usually noted: atrophy of the epidermis, hydropic degeneration of the basal cell layer, and edema of the epidermis with vasodilatation and extravasation of red blood cells. In older lesions hyperkeratosis and follicular plugging may be noted in addition to lymphocytic inflammatory changes with a peri-appendageal predominance. Fibrinoid changes are noted in the ground substance. Arteries show hyaline and fibrinoid necrosis of the media, frequently associated with intimal and adventitial proliferation and lymphocytic infiltration. Thrombi and infarcts may be present.

Direct immunofluorescence is most useful in the diagnosis of lupus erythematosus. Immunoglobulins, predominately IgG, and complement are bound to the region of the dermal-epidermal junction in skin lesions of lupus erythematosus. Homogenous, granular and thready patterns have been described (Figure 4).[34]

In systemic lupus erythematosus, the band may be seen in clinically uninvolved skin as well as in involved areas, whereas in discoid lupus erythematosus only the lesions are positive.[35] Antibodies to basement membrane or circulating antigen-antibody complexes due to exogenous or autologous antigens may be responsible for the deposition.

Dermoepidermal deposition of immunoglobulins is found in all cutaneous lupus erythematosus lesions and can be a diagnostic help. The test is extremely useful in confirming a diagnosis of systemic lupus erythematosus in patients without lupus erythematosus skin lesions. The presence of the band in clinically normal skin suggests greater severity of the disease.

Management of the Patient with Lupus Erythematosus

Lupus erythematosus can be a rapidly progressive fatal illness. More commonly, it is a chronic debilitating disease. Those with cutaneous lesions and systemic disease should be counselled as to prognosis, appropriately studied and referred when necessary. Their complex problems should be shared with those physicians best able to handle the complicated situations which may arise.

In some patients only cutaneous lesions occur. Therapy should be conservative. All patients with LE should avoid *excessive* sun exposure. A common error in management is to excessively frighten the LE patient concerning sun exposure. In most patients, moderate sun exposure can be tolerated. Photosensitivity can usually be determined by history. Sunscreens should be used when exposure is anticipated.

Topical corticosteroids are simple and effective therapy, particularly for early skin lesions. The fluorinated corticosteroids are most effective. Occlusion with a pliable plastic film increases absorption of corticosteroids and is often worthwhile (Figure 5). Intralesional corticosteroids are occasionally useful in refractory lesions.

For many lupus patients, the problem is primarily cosmetic. Elaborate, expensive work-ups may be indicated, but the patient's cosmetic problem must be considered. A useful adjunct is the use of make-up such as Covermark (Figure 6). Wigs also are of great help. For those patients whose lesions do not respond, antimalarial therapy should be considered. Adverse medicolegal considerations, reflecting adverse side-effects, have made many physicians reluctant to use antimalarials. Three antimalarials; chloroquine diphosphate, hydroxychloroquine sulfate, and quinacrine are used. Hydroxychloroquine is safer than chloroquine; its effectiveness is less. One or two tablets daily are given initially, and the dose is lowered when the patient responds. Side effects include gastrointestinal disturbances, itching, leukopenia, and thrombocytopenia. Pigmentary changes of the skin, hair, nails, and hard palate are noted occasionally, and suggest the possibility of retinopathy.[37] Occular changes include keratopathy and retinopathy. Ophthalmological consultation should be obtained before therapy is begun, and every three to six months thereafter.

Systemic Disease. Initially an assessment of disease activity is made. In addition to the usual studies, antinuclear antibodies, antibodies to DNA, RNA and ENA and serum complement values often correlate well with disease activity. Deposition of immune complexes in normal skin demonstrated by immunofluorescence, may be useful in predicting the presence of renal disease.

The patient must not be frightened, and prognosis and management should be discussed. Fatigue should be avoided. Antibiotics should not be given unless indicated. Drug reactions are common; drug therapy should be conservative. Salicylate alone may be indicated in patients with mild disease. Coated and buffered preparations are used. Adrenocortical steroids are necessary in patients not controlled by rest and salicylates. In patients with mild disease a small dose, i.e., 10 to 15 mg of prednisone per day is utilized. Corticoids are always administered to patients who are seriously ill. Thrombocytopenia, hemolytic anemia, neuropathy, pleurisy, pericarditis, and central nervous system involvement are other indications.[38] In severely ill patients a large initial dose, i.e., prednisone 60 to 100 mg or even more daily is given. The dose is increased until control is achieved, and is then decreased. A single daily dose, usually in the morning, perhaps is most advantageous. Alternate day dosage is rarely effective in the seriously ill patient. Side effects of steroids are well known and are usually proportional to the dosage given. Psychological dependence on steroid's euphoric side effect has been reported.[39] Depression is a frequent concomitant of chronic serious disease. In stressful situations, such as operation or infection, the dose of steroid is increased. Antimalarials may be useful in lowering the steroid requirement in SLE.

There is great interest in the use of immunosuppressive agents, particularly in the therapy of lupus nephropathy.[40-42] In addition, patients in whom steroid side effects or steroid failure are a problem are candidates for immunosuppressive therapy. Approximately 50% of patients with systemic lupus develop clinical evidence of renal disease, and about one half of these succumb to uremia resulting from lupus nephritis. Immunosuppressive agents are still experimental and should be used only by experienced clinicians. They have both immunosuppressive and anti-inflammatory effects. Antimetabolites such as 6-mercaptopurine and azathioprine, the alkylating agents such as cyclophophamide and nitrogen mustard, and folic acid antagonists such as methotrexate have been used.

Pregnancy and LE

The problems of birth control, pregnancy, and childbirth must be discussed with the female LE patient. Birth control pills should be used with caution, if at all. Other methods of birth control are preferable. Reports of exacerbation of LE associated with use of the pill are available. The advisability of a possible pregnancy is often a problem. The patient must be individually advised. Fertility is not affected, but the abortion rate is approximately twice that of the normal population. Full-term babies are usually unaffected by the disease. Steroid therapy is usually not harmful to the fetus. Maternal LE factor and ANA can be transmitted placentally, but they disappear permanently by the age of four months. Newborn infants of LE mothers rarely demonstrate the features of discoid or systemic LE.[43] However, patients are reassured that they need not be concerned about their children having the disease.

The patient's disease may remain the same, exacerbate, or go into remission during pregnancy. More commonly there is a deleterious effect. The vast majority of women with SLE tolerate pregnancy well, however, there are occasional tragic results. Women with systemic lupus erythematosus contemplating pregnancy are usually given an optimistic outlook if their disease is mild.

Scleroderma

Under this label are included disease processes varying from the sclerosis of a bit of skin to overwhelming systemic reactions terminating in rapid death. Scleroderma can be classified into two types—localized or cutaneous, and systemic.

Localized Cutaneous Scleroderma

The lesions begin as indurated areas which are faintly purplish. Their surface is usually smooth and shiny. Lesions may be multiple. Eventually, the induration decreases leaving a brown pigmentation which may be persistent. The usual duration is three to five years, but some lesions last longer. About a third of the patients have persistent residual pigmentation. Guttate morphea is simply a variant in which the lesions are smaller and more numerous. A history of trauma is usually not present. Patients with generalized morphea rarely develop systemic scleroderma.

Linear scleroderma usually involves the scalp, face, or an extremity. It is often associated with atrophy of the underlying structures. In the "en coup de sabre" form of linear scleroderma there is a linear depressed groove in the frontoparietal region which may extend into the scalp and down to the chin and neck. It may occur with facial atrophy. The bones of the skull may be affected and the electroencephalogram may show dysrhythmia. This disease can be a most disturbing cosmetic problem because of asymmetric development. Patients with linear scleroderma should have skull films, electroencephalography, and neurologic examinations. In other forms of linear scleroderma, bony defects of the spine are frequently noted, and neurological consultation should be obtained.

It is possible that localized scleroderma is related to systemic scleroderma as discoid lupus erythematosus is related to systemic lupus erythematosus.[44]

Systemic Scleroderma

Systemic scleroderma is a disease of unknown etiology in which pathological changes of the cutaneous, gastrointestinal, vascular, pulmonary, cardiac, and renal systems occur.

Clinical Features

The earliest clinical sign usually is Raynaud's phenomenon. Other common initial complaints include migratory arthralgia, thickening of the skin of the fingers, swelling of the hands, and ulcerations of the digits. Gastrointestinal disturbances include: dysphagia, regurgitation, weight loss, malabsorption and constipation.

There are three cutaneous findings in scleroderma: edema, sclerosis, and atrophy; most patients are seen in the sclerotic phase. The hands and face are most frequently involved (Figure 7). The skin of the face is smooth and shiny. The nose is small and pinched. The mouth is constricted. The fingers show atrophy, swelling, sclerosis, paronychia, and ankylosis. Digital ulcers are usually painful and slow to heal. Calcinosis cutis is present in 10% of patients (Figure 8). Calcinosis is a late sequela of scleroderma and occurs an average of 11 years after the onset of the disease.[45] Pigmentary changes occur in about 50 percent of patients. Both hyperpigmentation and depigmentation occur, the latter usually as scattered small areas (Figure 9). Cosmetically this can be a major problem. Telangiectasias are noted in many patients, usually in late stages of the disease. Multiple lesions are seen on affected patients, usually on the face and extremities and occasionally on the mucous membranes (Figure

10). The term "CRST syndrome" has been used to denote those patients with calcinosis. Raynaud's phenomenon, sclerodactyly, and telangiectasia.

Systemic Manifestations

Seventy-five percent of patients have esophageal involvement.[46] Esophageal reflux and dysphagia are the most common symptoms. The radiological appearance is that of an atonic, dilated esophagus. Stricture of the lower end of the esophagus and hiatus hernia frequently occur. Malabsorption may occur and is due to atonic intestinal loops with bacterial overgrowth as is also found in the blind loop syndrome. Clinical features include diarrhea and weight loss. These patients may improve dramatically with broad-spectrum antibiotics therapy. Paralytic ileus and death can occur as a result of gastrointestinal involvement. The liver is usually normal, though biliary cirrhosis is occasionally present.

Pulmonary symptoms, include progressive exertional dyspnea and cough. Abnormalities of pulmonary function tests are found in 70 percent of patients.[47] The usual changes are a diffuse, reticular fibrosis in the lower two thirds of the lung.

Pathologic changes in the kidney are frequent, although only a minority of patients have clinical renal disease. Renal failure is a common cause of death in scleroderma. The first clinical feature is slight proteinuria. The nephrotic syndrome may occur. The classic form of scleroderma renal disease is characterized by seizures and rapid death. The onset of renal involvement in scleroderma is always of grave significance and most patients die within weeks or months of renal involvement. There are no clinical or laboratory signs of value in determining which patient may develop renal scleroderma.

Muscle involvement occurs and may make differentiation from dermatomyositis difficult. Arthritis is common. The radiographic changes are indistinguishable from those of rheumatoid arthritis.

Laboratory Studies

The diagnosis of scleroderma is almost always made clinically. In the early stages laboratory examinations are helpful. They also help in evaluating the activity of the disease. The most helpful laboratory findings include: (1) decreased esophageal motility, (2) pulmonary fibrosis, (3) cutaneous sclerosis on biopsy, and (4) diminished intestinal absorption.

The blood count is rarely abnormal, but occasionally the sedimentation rate may be elevated or a mild hypochromic microcytic anemia may be present. A false-positive serology occurs rarely. Cold agglutinins and rheumatoid factor are present in one third of the patients.[46] Antinuclear antibodies have been demonstrated in 30 to 78 percent of patients.[48] The homogeneous pattern is seen most frequently. Nucleolar staining is seen much more commonly in this disease than in any other. Urinalysis can reveal albuminuria and microscopic hematuria. Evidence of malabsorption includes a flat glucose tolerance test, decreased d-xylose absorption, disturbed vitamin B-12 absorption, low serum carotene, and increased fecal fat.

Course and Prognosis

The course is variable; some patients die within a year. Most have a chronic course; increasing morbidity is usual. Cutaneous sclerosis may become very extensive. Articular disability is common. Limitation of motion ranges from ankylosis of the hands to generalized contractural deformities. Cardiac and renal lesions occur and indicate a poor prognosis. Thirty percent of patients have a fulminating course and die within five years of diagnosis; 70 percent have a slow course with progressing morbidity and disability. Rarely, the disease may become inactive.[46] Causes of death include intercurrent infection, respiratory, cardiac or renal failure, and perforation of the gastrointestinal tract.

No specific treatment is available, and therapy is supportive. General measures include avoidance of smoking and cold weather. Trauma to the hands should be avoided. Physiotherapy, including whirlpool, casts, traction splints, paraffin casts, massage and exercise, may be helpful. Early careful care of digital injuries with topical antibiotics is useful.

Salicylates can be used for mild polyarthritis. Sympatholytics may be helpful early, before organic changes in peripheral vessels occur. Phenoxybenzamine hydrochloride (Dibenzyline) and tolazoline (Priscoline) have been used. Reserpine may also prevent vasoconstriction. Intra-arterial reserpine has been used. Low molecular weight dextran may increase digital blood flow, heal ulcerated fingers, and decrease ischemic pain.[49]

The complications of long-term steroid programs are well known. Nonetheless, in those patients with debilitating arthritis, sclerodermatomyositis, extensive cutaneous edema, severe recurring digital ulcers, and acute toxic phases of the disease, corticosteroids may be utilized. We treat approximately one fourth of our adult patients with long-term, low-dosage corticosteroids, e.g. 15 mg. of prednisone, every other day. There are no major guides that one can follow. Many other pharmacologic treatments have been used without effect, including, epsilonaminocaproic acid, sodium versenate, PABA, nicotinic acid, and antihistamines. None of these agents is thought to alter the course of scleroderma.

Recent approaches are the use of antimalarials, low-molecular weight dextran, penicillamine and immunosuppressive drugs. Until further experience is accumulated, use of these agents should be restricted to those doing carefully controlled therapeutic studies.

Cervical sympathectomy is rarely, if ever, indicated in systemic scleroderma. The procedure can be difficult for the patient, and results usually are transient. Occasionally amputation of malformed, chronically infected, ulcerated digits is indicated. Calcium deposits can be excised if they cause pain or secondary infection.

Treatment of gastrointestinal symptoms is frequently effective, and should be directed toward controlling the gastric acid content of the esophagus. A bland diet and anatacids are used. Frequent small feedings, omission of late meals, and raising of the head of the bed to prevent gastric regurgitation are helpful. Dilatation of an esophageal stricture may be necessary to maintain an adequate lumen. Malabsorption syndrome should be treated with multivitamins, broad-spectrum antibiotics (tetracycline), and antidiarrheal agents.

Dermatomyositis

Dermatomyositis is an inflammatory disease of unknown etiology. It is a form of polymyositis, with involvement of the skin as well as the striated muscle. The onset of childhood cases is usually before the age of 10 years.[49] Adult cases occur predominately between the ages of 40 and 60. There is no sex predilection.

Familial occurrence is unusual.[50] Some cases follow infection. Immunological theories of etiology have been suggested. Paramyxovirus-like inclusions have been demonstrated and suggest a viral etiology.[51] The incidence of malignancy in adult cases varies from six to 52 percent. In our experience it is above 30 percent. The primary tumor may occur in the lungs, breast, stomach, rectum, kidney, testes, or uterus. Dermatomyositis has also been associated with the reticuloses including Hodgkin's disease, lymphosarcoma, and reticulum cell sarcoma. Dermatomyositis can appear briefly before the discovery of carcinoma. Recurrence following ablation of the tumor may indicate tumor recurrence.

Clinical Features

Presenting symptoms usually consist of stiffness, muscle weakness, and cutaneous lesions although either cutaneous signs or muscle involvement may be absent in individual cases. The classic cutaneous change is the heliotrope erythema of the upper eyelids, upper cheeks, and forehead (Figure 11). Facial telangiectasia and periorbital edema occur. Later, erythema of the hands, arms and upper back can develop (Figure 12). Erythema of the extensor surface of the joints of the knuckles, elbows and knees is often present. Subcutaneous edema may occur over the affected muscles.

Calcinosis is present most commonly in children and occurs in approximately 50 percent as small nodules in the shoulder and pelvic girdle area.[52] The calcium may ulcerate and extrude.

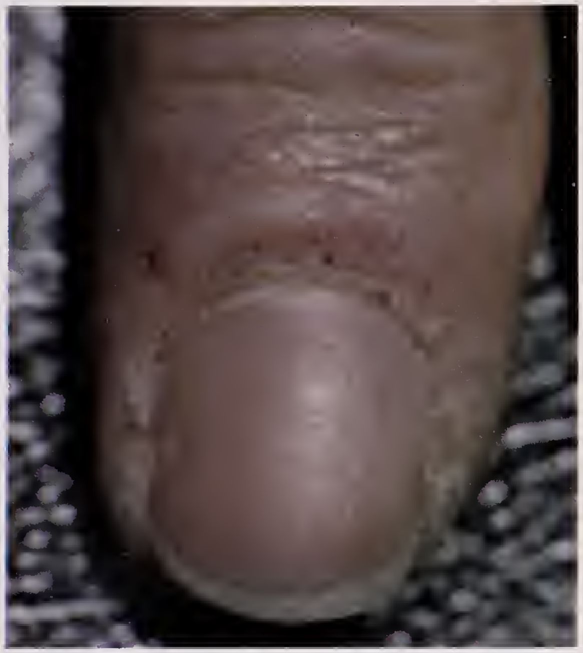

Fig. 12—Paronychial linear telangiectasia in a patient with dermatomyositis.

Children tend to have a disseminated form of calcification; in adults it is more localized.

Treatment

Muscle pain and weakness affect primarily the proximal limbs and neck flexors. Involvement of the pelvic and shoulder musculature usually is severe. Flexural contractions of the elbows, hips, knees and ankles are prominent. Hypopharyngeal involvement with diminished deglutition is a serious prognostic sign. The palatal, pharyngeal, and upper third of the esophageal musculature are also affected. with aspiration pneumonia a serious problem.

Other organ systems can also be involved. Clinical signs include impaired activity of the small intestine; respiratory difficulty secondary to intercostal and diaphragmatic weakness, and pulmonary hypertension or cor pulmonale. Gastrointestinal ulcerations are secondary to vasculitis. Melena, hematemesis, and abdominal pain are common in the childhood form.

Laboratory Findings

The sedimentation rate may be elevated during the active phase. Eosinophilia may be present. Creatinuria may be present, and the 24-hour urinary creatine is a useful test in evaluating disease activity. Serial studies of muscle enzyme levels are useful in determining disease activity. These include creatine phosphokinase (CPK), glutamic oxaloacetic transaminase (SGOT), aldolase, and lactic dehydrogenase (LDH). They are increased in acute inflammatory muscle lesions. It is important to rule out hepatic and cardiac disease when interpreting enzymes. Muscle enzyme levels normalize faster than muscular function or the electromyogram. In patients with chronic dermatomyositis, the enzyme levels may be minimally elevated or normal.

Electromyography is useful to determine the site of biopsy and distinguish myopathy from neuropathy. It should always be performed. Xrays of the muscles may demonstrate calcinosis, particularly in the gluteal muscles.

Skin and muscle biopsies are helpful procedures in confirming the diagnosis. Proximal muscles, usually the anterior thigh or deltoid, are best; the site should be determined by EMG. The histopathological changes in the muscle are not specific and can be similar to changes noted in other types of polymyositis and other collagen diseases. There is infiltration of polymorphonuclear lymphocytes and plasma cells and scattered areas of atrophy. Hyalin thrombi may occur.

Course

The course is variable and unpredictable. The acute phase may become quiescent and result in only minimal changes, or may become fulminant, with death ensuing within the first year. Some patients develop disabling contractures or extensive calcinosis. Sheard[53] reported 25 patients, of whom 13 died after an average course of 20 months. In Everett and Curtis' series of 19 patients, four died within the first year.[54] Their deaths were secondary to hypopharyngeal paralysis or cardiac involvement or both, whereas those who died after the first year usually died from pneumonia. Death can also occur from steroid or immunosuppressive side-effects.

Treatment

Early diagnosis is essential. Laboratory tests must be utilized to ascertain disease activity. During the early stages of active disease relatively high doses of corticosteroids, i.e., 25 to 75 mg. of prednisone daily, are necessary. Thereafter the dose can be tapered, depending on the response.

Steroids tend to produce improvement with decreased muscle pain and tenderness and increased muscle strength. Muscle enzyme levels decrease with clinical improvement. The disease is usually chronic and therapy is required for months or years. Some do not feel that steroids produce dramatic improvement and question the advisability of using them. In one study, eight children treated with steroids did not manifest an altered course.[54] In adults, steroids are certainly indicated. Weakness can also arise from maintenance dosages of corticosteroids, as a result of either steroid myopathy or hypokalemia. This may be difficult to differentiate clinically from an exacerbation of the disease.

Management of calcinosis is difficult. Chelating agents have been used with disappointing results.[55] Physiotherapy may help prevent contractures. Immunosuppressives have been used in some patients but must be considered experimental at this time. When patients are unresponsive to steroids or have severe complications, immunosuppressives can be utilized. Methotrexate, cyclophosphamid and azathioprinine have been primarily used with good results.[56]

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advisable to explain carefully the proper home use of ultraviolet light therapy. Because the dose varies inversely with the square of the distance from the lamp to the skin, the distance must be kept the same for each exposure. Only the time will be varied. The patient should start with a short time and increase each day until a mild burn occurs. Then one to two treatments per week are usually satisfactory. The time of exposure will have to be increased periodically to obtain a mild burn. Most dermatologists do not feel that a suberythema dose is of value. The eyes must be shielded by sunglasses or other opaque material. It is advisable to have an alarm timer and ideally another person in the vicinity to double check that the patient has not fallen asleep istries monitoring liver and renal function.

Patients often ask about the danger of skin cancer developing from ultraviolet treatment for acne. Long continued daily exposure over many years, e.g., farmers and sailors, can cause skin cancer. However, limited weekly or twice weekly exposure for a few months to several years has not been shown to be harmful. Naturally, patients who have a history of adverse reactions should not be treated with ultraviolet light.

(b) Cryotherapy: Pieces of dry ice alone or dry ice-sulfur-acetone slush have also been used as a drying-peeling agent.

(c) Antibiotics: Whereas acne surgery and the drying-peeling agents are effective in managing less inflammatory forms of acne, specifically blackheads and whiteheads, broad spectrum antibiotics, especially the tetracyclines, are usually effective in the treatment of inflammatory papules, pustules, nodules and cysts[9] (Figures 2 and 4). Systemic antibiotics should be administered *only* to patients who do not respond to milder, topical forms of therapy described above. A typical tetracycline regimen consists of 250 mg. p.o. b.i.d. for three weeks or longer until a positive result is obtained, followed by gradual reduction to the lowest dose sufficient to maintain control. Further cuts or cessation of therapy must be attempted periodically. It may be necessary at times, to return to higher dosage temporarily, but overall this is the only way to use the smallest necessary maintenance level. Because the sebaceous gland appears to act as an excretory route for tetracycline, this maintenance may be as low as 250 mg. p.o. q.o.d. Tetracycline should be taken on an empty stomach, e.g., one-half hour or more before meals or one to two hours after meals.

Although these low levels of tetracycline, even in long-term therapy, are relatively free from toxicity, an awareness of possible side effects is mandatory. This includes discoloration of deciduous and permanent teeth from the fourth fetal month through the twelfth year of life—therefore, tetracycline is not used in pregnant women or in children; possible liver damage, especially in the presence of renal disease; anaphylactoid reactions; nausea; diarrhea; and yeast superinfections. Some authorities advocate a laboratory checkup at the end of each six months of continuous or 12 months of intermittent, tetracycline therapy. This should include white blood count, hemoglobin, routine urine exam and some blood chemistries, monitoring liver and renal function.

In tetracycline-resistant patients, erythromycin and clindamycin may be effective, but must, of course, be used judiciously.

(d) Corticosteroids: Intralesional injection of corticosteroids such as hydrocortisone acetate or triamcinolone acetonide or acetate in appropriate concentration (0.05-0.20 ml of 10 mg/ml) is known to be an effective means of improving inflammatory papules, nodules and cysts, as well as reducing scarring. Occasional reversible atrophy may occur which is the reason for using small amounts in low concentrations as above. Topical steroids seem to be ineffective in acne.

Systemic corticosteroids are reserved for use only in rare cases of severe flaring of nodulocystic acne, because of their hazardous side effects and their ability to produce acne lesions themselves.

(e) Cyclic Estrogen-Progestin Therapy: The use of cyclic estrogen-progestin therapy ("oral contraceptives") in selected female patients is based on the possible role of hormonal control in the pathogenesis of acne.[10] As mentioned above, estrogens suppress sebum formation, probably by inhibiting androgen production. Because of the possibility of increased thromboembolic phenomena, as well as a multiplicity of other side effects, including premature cessation of bone growth, nausea, weight gain, spotting, breast tenderness, amenorrhea and chloasma, such hormonal therapy must be used with caution. Oral contraceptives should be administered in conjunction with gynecologic consultation and should never be used before age 16 years, when maximum bone growth is obtained.

These agents are administered cyclically for three-week periods. Treatment is begun on the fifth day of menses and continued daily for 20 to 21 days. Following discontinuation of medication, bleeding ensues within a few days, and medication is renewed on day five as in the previous cycle. If withdrawal bleeding has not occurred by the seventh interval day, the medication is then restarted. The agents used for adequate sebaceous gland suppression should contain up to 0.1 mg of the estrogen, ethinyl estradiol, or its 3-methyl ether derivative, mestranol. In general, the effectiveness of this therapy parallels the amount of estrogens present in the medication. The amount of progestins in these medications does not seem to be important in acne therapy.

It may take three to four cycles for clinical improvement. If the lower dose estrogens (50 μmg) are ineffective, then the higher dose (80 μmg) should be used. In an occasional patient, the acne will flare early in the course of treatment, especially if the progestin has androgenic activity, e.g., norgestrel.

(f) Diet: Dietary management appears to be of little value in the treatment of acne. Occasionally a patient will have his disease aggravated by the ingestion of certain foods, especially chocolate. There is no scientific evidence that any group or type of food is particularly harmful, and most patients will tolerate all foods without ill effect on their acne. If a patient feels certain that a given food aggravates his acne, then advise him not to eat it.

(g) The role of tension in acne is unproven. Because of uncertainty about the natural course of this disease, and the difficulty of adequately measuring psychologic stress, it has been impossible to correlate tension and acne on a controlled basis. There is some experimental basis for correlating stress with adrenal cortical production, and this could indirectly cause acne. However, this last step has not been proven satisfactorily on a clinical basis. Although most physicians and many patients feel that such a correlation exists.

If the physician feels there is a relationship between acne and stress, then this should be presented to the patient, especially adolescents, with the explanation and reassurance that stress is to a large extent normal at that age. There are many readjustments and conflicts in the teenager (social, political, family adjustments, sexual, economic, educational, etc.). Fortunately, many of these problems are more easily handled by the patient as he matures. In many cases, reassurance alone can help patients cope with their acne.

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Common Baldness

SIGFRID A. MULLER, M.D.*

Common baldness represents 99% of all types of scalp alopecia. Its development is dependent on the presence of sufficient androgens, aging, and a hereditary component most commonly believed to be transmitted as an autosomal-dominant characteristic. The condition usually is milder in women in whom a diffuse alopecia is seen primarily involving the frontocentral scalp and rarely progressing to a completely bald scalp. There is no known medical treatment.

MANY SYNONYMS have been used for common baldness, especially seborrheic alopecia, pattern alopecia, and premature alopecia, all of which have emphasized a variably important clinical characteristic. Objections to these terms have been made because none were exclusive. Thus, the condition was not related etiologically to seborrhea and was not always premature. Also, patterns of alopecia were not uncommonly seen in other disorders and were less obvious when seen in women. Common baldness is an appropriate term that sufficiently characterizes the type of alopecia without emphasizing unduly any particular clinical characteristic. Hamilton[1] has indicated that it represents 99% of all types of scalp alopecia. Androgenetic alopecia is also a useful name because it emphasizes the important association of androgen dependency and a hereditary component in the causation of the hair loss, but because it is not understood by the general public, it is less desirable.

Clinical Features

Although everyone is familiar with common baldness, diagnosis may be difficult when the condition is mild, early in its course, or appears late in life. Certain clinical aspects, particularly the clinical appearance, time of onset, progression, and severity of the alopecia, are usually significantly different in women.[2]

The onset of thinning and increased shedding of scalp hairs usually is gradual, but some patients experience a rather sharply delineated onset. In men, the anterior hairline recedes gradually, es-

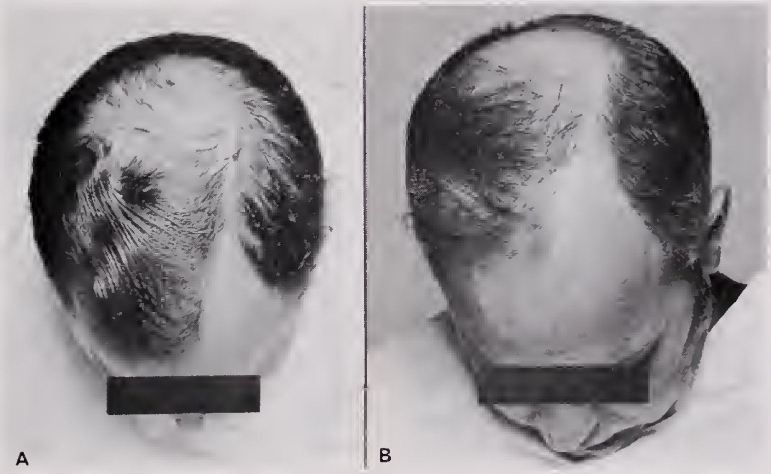
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Fig. 1—Progression of common baldness in (A) 34-year-old man and (B) nine years later.

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Presented at the Minnesota Academy of Family Physicians Refresher Course, Bloomington, Minnesota, April 17 and 18, 1974.

pecially in the parietal regions, so that an M-shaped anterior recession frequently is followed by the development of a bald spot on the posterior crown (Figure 1). When the hair loss is more severe, enlargement and confluence also occur so that in approximately 15% of men only a peripheral fringe of scalp hair remains.

In women, common baldness begins later in life, generally, when they are in their mid-twenties; but usually they do not seek medical consultation until a decade later. Thinning and increased shedding of hairs is more diffuse and milder, involving the frontocentral scalp primarily and sparing the peripheral margins of the scalp. The parietal recessions are usually not prominent, and severe thinning is infrequent. A bald pate is rarely seen except in association with idiopathic hirsutism or in pathologic disorders related to increased androgen stimulation. Thus, male-type common baldness in a woman should alert the physician to test for an endocrine abnormality.

Examination of plucked hairs obtained by the methods of Van Scott et al[3] from the affected scalp is not diagnostic, but the hairs frequently vary greatly in thickness and the thinner hairs are hypopigmented. The numbers of telogen hairs are usually slightly to moderately increased as the duration of the anagen phase is decreased, resulting in shorter hairs that pass into the telogen phase more frequently.

A biopsy specimen of affected scalp is also not helpful in establishing the diagnosis except that examination might exclude other possible conditions for the hair loss. The histopathologic findings are those of an ascending obliterative fibrosis of the connective tissue sheath of the hair follicle. The changes are subtle, easily missed in the earliest stages, and readily confused with the findings of normal aging.

Endocrine Aspects

Common baldness does not occur in men who fail to mature sexually and can be induced by giving testosterone to eunuchs who are genetically susceptible. Likewise, susceptible women can develop male-type common baldness when given testosterone. The mild diffuse types of common baldness seen in women and the failure to progress to more severe loss of hair have been related to the lower levels of androgen found in women. This is suggested by the development of male-type common baldness in susceptible women treated with testosterone.

It is postulated dihydrotestosterone is the intracellular effector of testosterone action in the target tissue. Regional differences in the ability of skin to convert testosterone to dihydrotestosterone, which is a much more potent androgen, have been confirmed. The paradoxic reaction of androgens causing baldness in genetically sensitive areas of the scalp and stimulation of hair growth or hirsutism in other regions of the body should be noted. This has been postulated to be related to differences in the metabolism of testosterone by the individual hair follicle. In one scheme, dihydrotestosterone causes inhibition of adenyl cyclase in the follicle, a decrease of intracellular cyclic-AMP, and consequent inhibition of energy production and protein synthesis in the hair. The end result is the premature termination of the growth cycle of terminal hairs and their transformation into vellous hairs.[4]

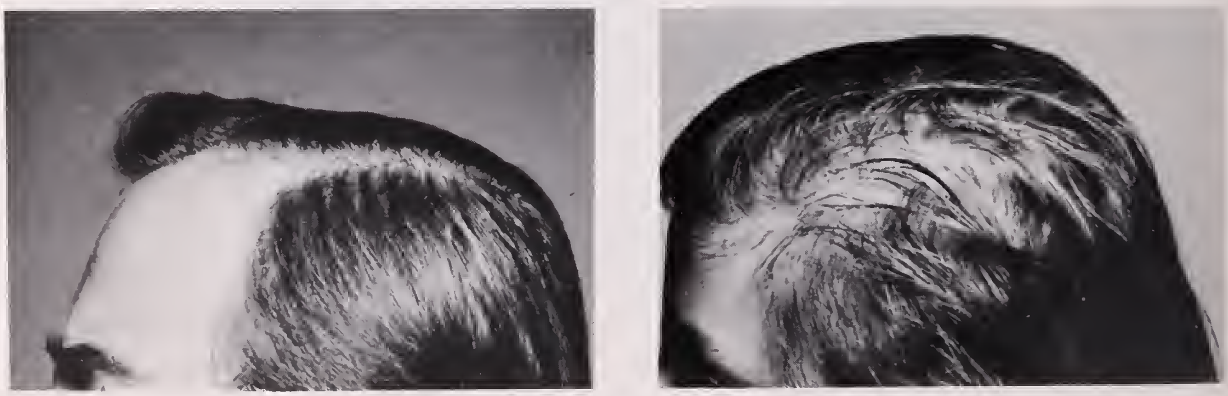

Fig. 2—(A-left) Mild common baldness easily overlooked in 49-year-old man. (B-right) 14-year-old son who developed common baldness at the age of 13. A strong family history of common baldness was present in both men and women among his relatives.

Prevalence and Heritability

Precise data on the prevalence of common baldness are not available because it is difficult to differentiate common baldness from thinning of hair normally seen in aged persons and because the condition cannot be confirmed in mildly affected persons. However, most studies have noted a prevalence of common baldness of 40 to 50% in young and middle-aged Caucasian men. Negroes are less commonly affected and American Indians, Orientals, and Eskimos least of all.[5]

Prevalence estimates in women are more difficult to determine because the condition is milder, and it is so readily masked. A prevalence of 25% seems reasonable for Caucasian women.

The mode of transmission of common baldness has not been settled, but autosomal-dominant inheritance with incomplete penetrance and variable expressivity is most commonly described (Figure 2). The weak point of any single gene hypothesis is the inability to determine the zygosity of affected persons as well as the identification of the condition in the very mildly affected persons. A multifactorial genetic mechanism akin to those for height and weight also has been suggested.[6]

Treatment

Affected persons frequently press their physicians for specific therapy even when they note that their physicians and their families may be similarly affected. There is no medical treatment for common baldness. The problem is compounded by the promotional gimmicks indicating an ideal state of hairiness that is not achievable because of the unalterable inheritance present and the resulting anxiety produced when the cosmetic appearance is less than this. Any scientific explanation has to consider the folklore of causation related to external agents and the worthless treatments propounded by lay hair experts. No one can make hair grow thicker or faster, and no amount of massage or ultraviolet light will make any difference cosmetically.

Avoidance of injurious cosmetic procedures such as bleaching, dyeing, and permanent wave solution as well as tight curlers may decrease the rate at which the fragile scalp hairs break. The use of so-called hair repair shampoos that coat the hairs with polypeptide residues may temporarily make the scalp hair look thicker. For the more severely affected persons, the use of full and partial wigs is the most practical recommendation for those who wish a cosmetic aid.

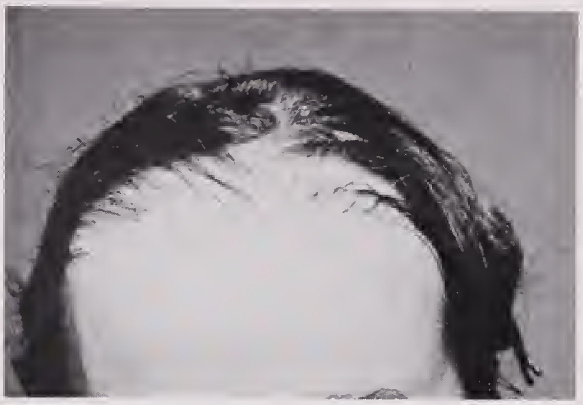

Fig. 3—Successful punch autografts with good hair growth in recipient sites at anterior hairline in 55-year-old woman, after five years. She had refused further therapy. Note hypopigmentation and atrophy of grafts. Male-type common baldness had been present for many years, and no endocrine abnormalities were found.

The finding that autografts of genetically nonsensitive areas of scalp (the lateral and posterior parietal and occipital areas) transplanted into the bald areas in common baldness will grow hair luxuriantly has provided an instant demise to the theories of circulatory deficiencies or of excessive tautness of the scalp as the causation of common baldness.[7] It has also provided a means of redistributing scalp hair follicles from the peripheral margins of the scalp, where hair growth is permanent, to the bald areas (Figure 3). The procedure is no panacea, but it can achieve cosmetically acceptable results when done in carefully selected, strongly motivated men. For the more severely affected persons, 100 to 300 punch autografts may be required. It is not, however, usually worthwhile in affected women.

In the final analysis, the careful clinical examination of the scalp, followed by examination of a hair pluck specimen (approximately 30 to 40 hairs) to exclude possible superimposed aggravants such as excessive breakage and drug-induced forms of alopecia, not only will establish the diagnosis but also will confirm the physician's competency and responsibility in this area. The findings also will facilitate the explanation to the patient who probably has considerable anxiety about his loss of hair. In particular, the physician should be sensitive to the emotional strain of seemingly minimal loss of hair in women who are terrified that they will become bald. For them, strong reassurance that this will not happen is important. The physician should be aware of the severe loss of ego that many patients feel; and he should not underestimate the impact that the patient believes the hair loss will have on his life. A sympathetic attitude, together with an explanation of the problem, will be of considerable help to most patients.

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Book Review

CONSULTATIONS IN DERMATOLOGY II with Walter B. Shelley. W. B. Saunders Co. Phila. 1974.

In this unusual book, Shelley, professor of dermatology at the U. of Penn., takes the reader on rounds with him visiting 50 cases in 50 short chapters. One doesn't cover all of skin in 332 pages and the reader will see described those situations particularly interesting to Shelley: Incontinentia pigmenti, atrophoderma (Pasini-Pierini), Porokeratosis of Mibelli for rarities; and for the common touch, leg ulcer, syphilis, and tattoo. Shelley writes well.* His descriptions stick to the ribs as for instance: "This lesion (keratoacanthoma) is the clinician's pride and joy. He exalts in his awareness of the benign nature of this malignant-appearing tumor . . ." A single papule makes the diagnosis in this disease!

One is walking on rounds with Shelley and would not expect his statements to have numbered bibliographic references. But he does include with each patient (chapter) a profusion of references each with a descriptive line, the pearl of the article.

Edward F. Glifort is the photographer. One picture goes with each chapter. These are in black and white uniformly handsomely photographed and printed, but a book on skin, or the dermatology special issue of a journal, demands color.

Reuben Berman, M.D.
Editor

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*See also page 773.

Psoriasis

CHARLES J. MCDONALD, M.D.*

Psoriasis is a chronic inflammatory and proliferative disease of the skin and joints. Cutaneous lesions predominate and respond to both topical and systemic agents.

PSORIASIS, USUALLY A chronic, though sometimes acute, inflammatory and proliferative disease of the skin, affects two to three percent of the United States population. It is a disease in which incidence is related to both genetic and environmental factors. Psoriasis is inherited as a single autosomal dominant trait with incomplete penetrance. That genetic factors play an important part in disease incidence may be demonstrated by the following. It has been estimated that the incidence of psoriasis in black Americans barely approaches 0.1 percent. The same incidence figures have been noted in native West African blacks. Most black Americans trace their origin to West Africa. Verhagen and Koten have shown that psoriasis is relatively common in black East Africans.[1] In fact, the incidence of psoriasis in East African blacks approaches 2.6 percent, exceeding the percent incidence as estimated by Farber, in the white American population.[2]

The early stage eruption may be nonspecific in appearance. In fact, early psoriasis is often confused with a variety of skin diseases, such as drug eruptions, dermatitis, insect bites and chicken pox. Early lesions are asymptomatic although some patients complain of mild pruritus. The initial lesion is an erythematous papule which may progress to pustulation, accounting for the confusion with chicken pox. Soon after the erythematous papules, the characteristic papulosquamous plaque appears. The typical psoriatic eruption consists of erythematous, scaling plaques of variable size. The lesions are, in most cases, symmetrical. Although psoriasis characteristically involves the extensor surfaces of the extremities, especially the elbows and knees, the earliest lesions may be confined to the intergluteal fold. The scalp, nails and genitals are also frequent sites of involvement. Most patients experience only a few lesions limited to the sites mentioned above, however, in a significant number the disease is extensive and may involve the entire body surface. Typical lesions of psoriasis may be seen in Figures 1A-1C.

A variety of skin lesions with different morphological appearances may be found in patients with psoriasis, giving rise to many descriptive forms, such as *psoriasis rupioides, psoriasis gutta,* and *psoriasis discoidea.* In spite of gross morphological differences, in each case the basic biological defect is the same.

Pustular psoriasis is a special type in which the characteristic lesion is a pustule rather than an erythematous scaling plaque (Figure 2). The pustules are most often confined to the palms and soles. Infrequently they are associated with psoriatic papules and plaques on other parts of the body. The pustules are sterile, representing collections of inflammatory cells within the epidermis. As will be discussed later, epidermal microabscesses are basic elements in the histopathologic picture of psoriasis. Thus, it becomes easy to envision a group of microabscesses coalescing to form macroabscesses and the clinically apparent lesions of pustular psoriasis.

The nail changes of psoriasis are characteristic, and in many cases provide the most significant clues to a definitive diagnosis. Punctate pits and ridges are almost always found in patients with psoriasis even in the absence of extensive skin disease. Separation of the nail from the nail bed, and subungal collections of a granular or powdery material are often seen. The number of nails affected in each patient is variable.

In patients with active psoriasis even slight trauma, sufficient to disrupt the epidermis and underlying dermis, will often result in the production of psoriatic plaques at the site of injury. This has been called the "Koebner reaction" or the isomorphic response. The trauma may be mechanical, infectious, a burn, etc. Acute guttate psoriasis is often associated with acute viral or bacterial (streptococcal) upper respiratory and systemic infections. The role of vascular damage in the production of psoriatic lesions is often cited to account for the lesions of guttate psoriasis.

Two severe types of psoriasis must be given special mention. They are erythrodermic psoriasis and pustular psoriasis of Zumbuch. Psoriatic

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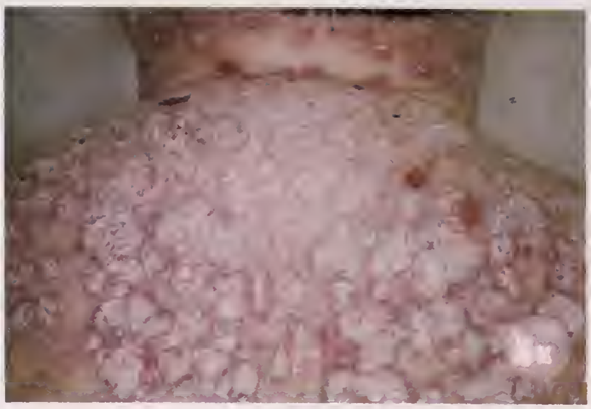

Fig. 1A—Psoriasis of back showing typical red plaques covered by silvery white scales.

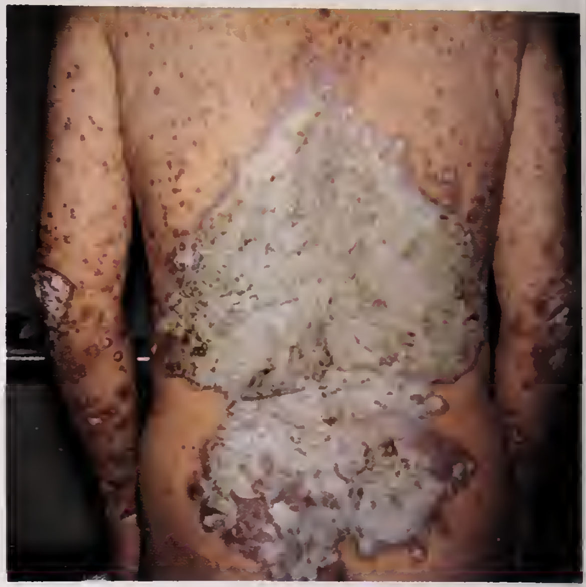

Fig. 1B—Patient with severe, total body psoriasis.

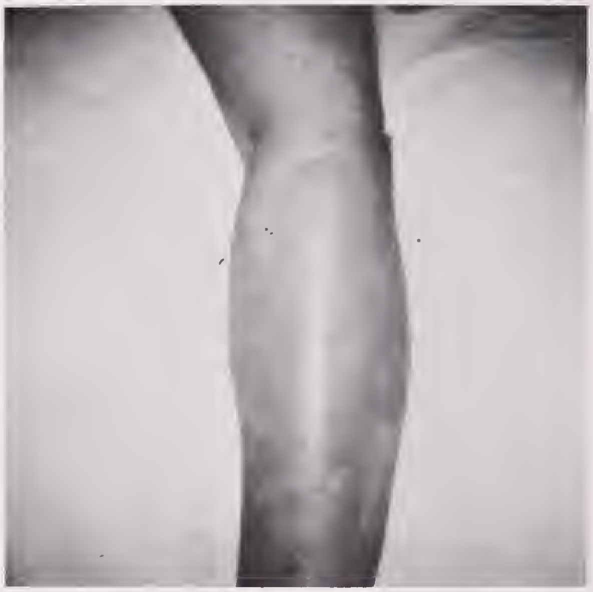

Fig. 1C—Psoriasis in a patient who spends the greater part of a day removing scales from the psoriatic lesion.

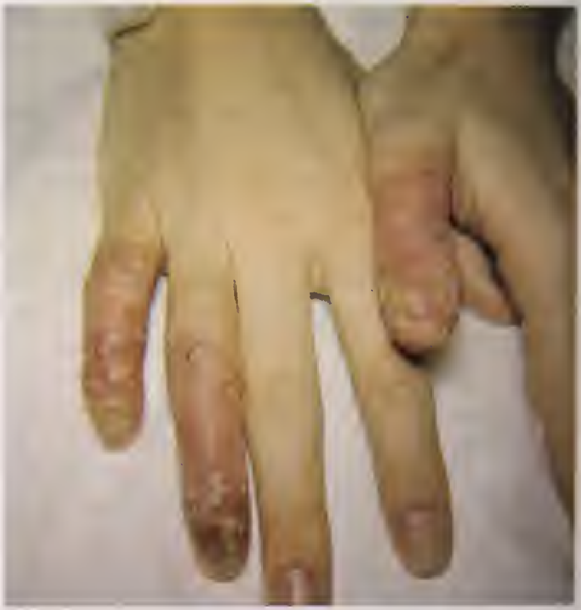

Fig. 2—Pustular psoriasis.

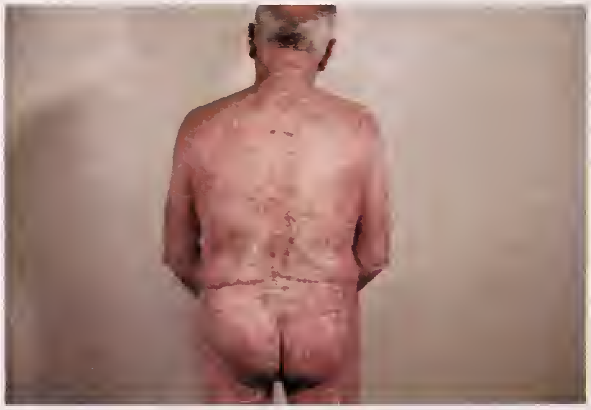

Fig. 3A—Erythrodermic psoriasis.

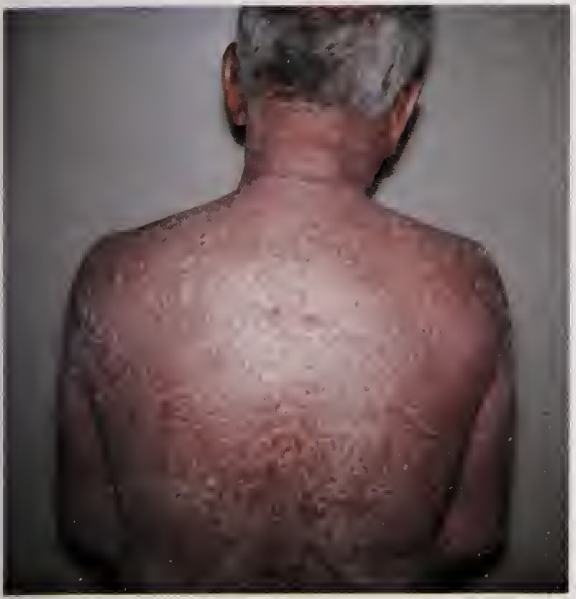

Fig. 3B—Erythrodermic psoriasis.

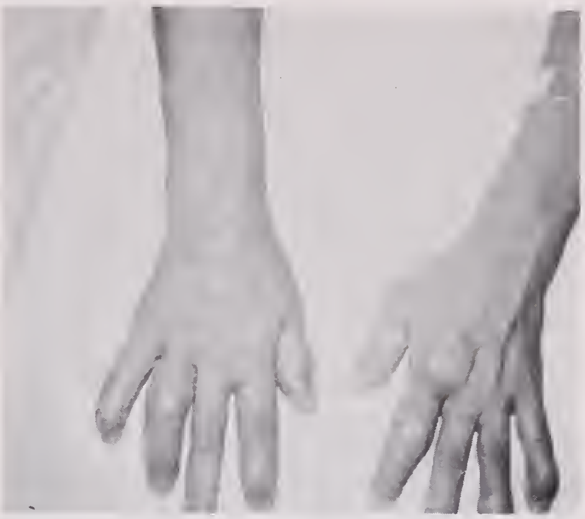

Fig. 4A—Psoriatic arthritis in a treated patient. Note the typical distal interphalangeal joint deformities and the "so-called' sausage shaped and swan neck deformities of the digits.

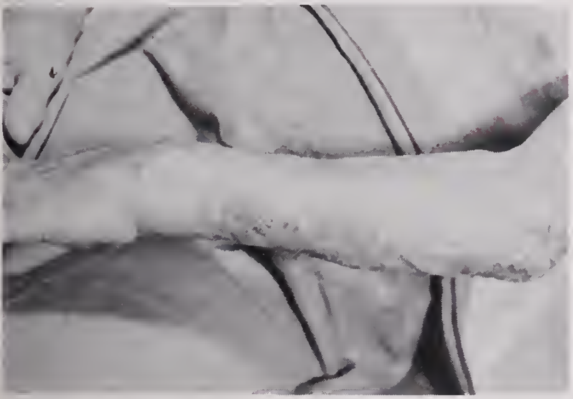

Fig. 4B—Severe psoriatic arthritis of the wrist.

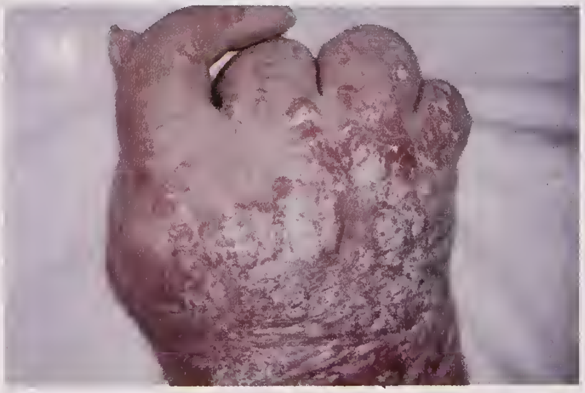

Fig. 4C—Severe residual joint deformities in a patient with psoriatic arthritis.

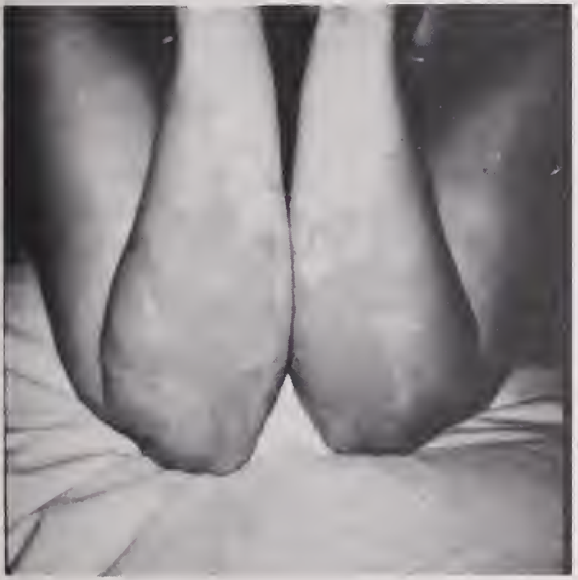

Fig. 5A—Before treatment with azaribine.

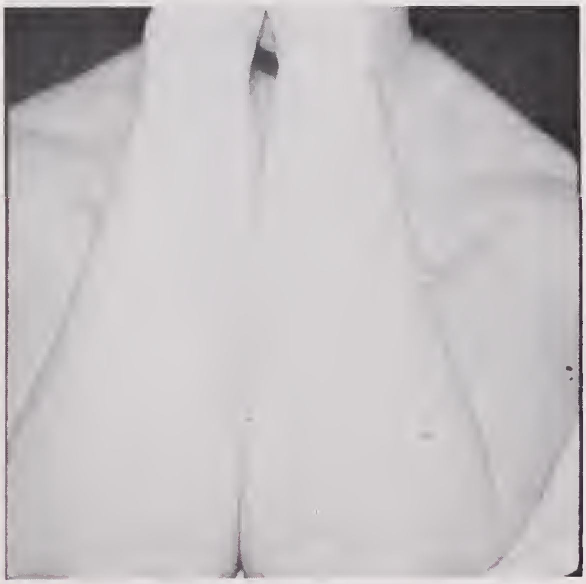

Fig. 5B—After 4 months treatment with azaribine.

erythroderma occurs most often with rapid progression and spread of psoriasis. Often generalized drug eruptions precipitate this form of psoriasis. Erythrodermic psoriasis frequently occurs in patients who have terminated systemic corticosteroid therapy. Patients with psoriatic erythroderma literally are one large psoriatic plaque. They are red and uncomfortable (Figures 3A and B). The skin loses large quantities of scales each day. Heat regulation through the psoriatic scales is very difficult, therefore, these patients complain constantly of chilled bodies. Often their lower extremities are edematous, probably related to the loss of intravascular proteins, not through the intact skin, but via the increased metabolic requirements of rapidly proliferating skin. Body stores of protein are depleted accompanied by loss of serum proteins and peripheral edema occurs.

Pustular psoriasis of Zumbuch is the most severe form of psoriasis. Patients die in nearly all cases that are improperly or inadequately treated. Patients with this form often require hospitalization as dermatological emergencies. The disease begins with the rapid onset of erythema around a chronic plaque, or erythema arises *de novo* and then rapidly involves the entire body. The surface of the erythematous skin is covered with two to three mm pustules. The skin is very warm to touch. Patients complain of malaise, chills, and fever. The total white cell count often rises to very high levels, mimicking that seen in acute febrile infections and acute leukemia. The rise and fall in white cell count, during active therapy, often serves as an index of response to therapy. Although temperature and white count elevations occur during episodes of acute pustular psoriasis, the cause of these elevations is not infectious. Therefore, patients will not respond to nonspecific antibiotic therapy, instead, they respond to specific treatment for acute psoriasis.

In as many as 25 percent of persons with psoriasis, there is associated polyarticular arthritis. Small joints of the hand and feet, such as the distal interphalangeal joints, are most frequently involved (Figures 4A-C), though, in a significant number of patients, larger joints of the cervical spine, sacrum, shoulder and pelvic girdles, and the knees may be affected. Destructive joint deformities tend to occur in the more severely affected persons. In fact, the skin and joint manifestations, singly or in combination, are often severe enough to cause crippling and complete debilitation.

Laboratory Aspects

Clinical Laboratory

Only a few laboratory studies are abnormal in psoriasis. Low serum albumin levels in psoriatic erythroderma, and high white blood cell counts in acute pustular psoriasis of Zumbuch have been discussed. High serum uric acid levels frequently occur and are probably related to increased protein metabolism. Gout infrequently occurs in psoriatic patients with elevated serum uric acid levels.

Patients with moderately severe to severe psoriatic arthritis often present with an anemia which is characterized by a low serum iron and low total iron binding capacity.

Pathology

The histological picture in psoriasis is quite characteristic. The epidermis is thickened (acanthotic), the number of epidermal mitotic figures are increased, the rete ridges are elongated and branched, and the suprapapillary portions of the malpighiian layer are thinned. There is absence of a granular layer in the epidermis, and the cornified layer is parakeratotic (nuclei are retained within the cells) and hyperkeratotic. Microscopic collections of white blood cells (microabscesses of Munro) are located in the keratinized epidermis. In the papillary dermis the capillaries are dilated and tortuous, and their walls are thickened. An inflammatory infiltrate of lymphocytes and histiocytes occupies most of the upper dermis.

Laboratory Investigations

VanScott and Ekel[3] and Rothberg and Crounse[4] have demonstrated that psoriasis, in addition to being an inflammatory disease, is a benign hyperplastic disease of the skin. Epidermal cells in areas of skin involvement have a very rapid rate of replication. The mitotic index of the germinative cell population per unit length of involved epidermis is increased, and there is a reduced epidermal cell transit time, or epidermal cell "turnover" time in involved areas.

Treatment

Topical

The multiplicity of therapeutic programs which have been recommended for the treatment of the various forms of psoriasis are indicative of the relative ineffectiveness of most. There is no known cure for psoriasis; all treatment programs are palliative, yet when used appropriately, can result in considerable relief of the signs and symptoms of disease, and in many cases can effect long lasting disease remissions. Often psoriasis disappears spontaneously without treatment. In most persons frequent recurrences are likely.

Mild cases of inflammatory psoriasis often respond to topical corticosteroid or tar preparations when applied three to four times daily. Tar baths, once daily, are recommended by many dermatologists. Intralesional injections of dilute solutions of parenteral corticosteroids are used to effect a complete resolution of lesions in patients with very limited disease. Topical corticosteroids applied under occlusive dressings for six to eight hours daily will sometimes inhibit the spread of, or cause resolution of psoriasis. This form of therapy must be used with caution in patients with total body disease because it may result in suppression of adrenal gland function. The use of topical corticosteroids with occlusion should be limited to short courses in any patient. Continuous use of the occlusive technique also leads to epidermal atrophy.

In a number of persons psoriasis is so severe and extensive that local measures described above will not effect a resolution of disease. Such patients usually require treatment with a modified Goeckerman regimen. A minimal care hospital facility or psoriasis day care center is ideal for this form of treatment.[5] In my institution, a preparation containing 3% Crude Coal Tar and 5% Salacylic Acid in petrolatum or a water washable base is applied to the total body except the face for at least one hour. The tar is removed with a light lubricating oil leaving a minimally perceptable layer of tar on the skin. The patient is exposed to a minimal erythema dose of ultraviolet light in a specially constructed light box. Most patients tolerate a beginning exposure time of 30 seconds which is sufficient to produce initial erythema. Light exposure is increased by 30 seconds each exposure which is given twice daily to a maximum exposure time of 12 to 15 minutes. One hour after light exposure the patient bathes to remove excess scales; tar is reapplied and the procedure is repeated in six to eight hours on the same day.

Systemic

In patients whose disease is severe and recalcitrant to the regimens outlined above and/or have severe debilitating arthritis, treatment with one of several antineoplastic agents may be indicated (Figures 5, 6, 7). *A word of caution; the management of patients with these potent drugs should be considered only by those who by virtue of training and experience, are skilled in their use, and who have extensive knowledge of the pharmacology and toxicology of each drug!* These drugs are very potent and toxic, and their use even

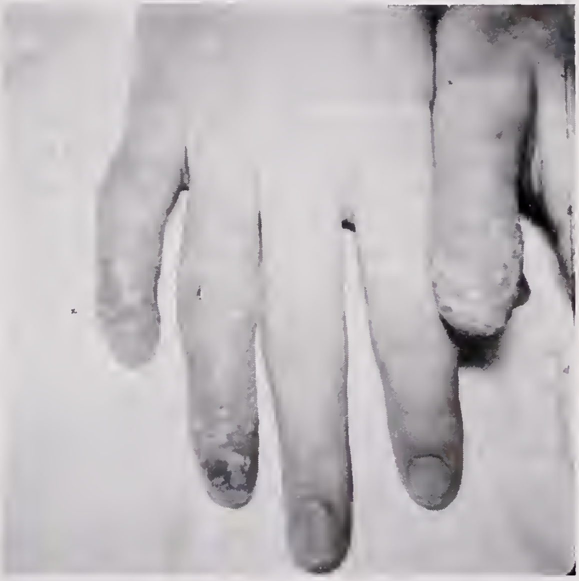

Fig. 6A—Pustular psoriasis before treatment with azaribine.

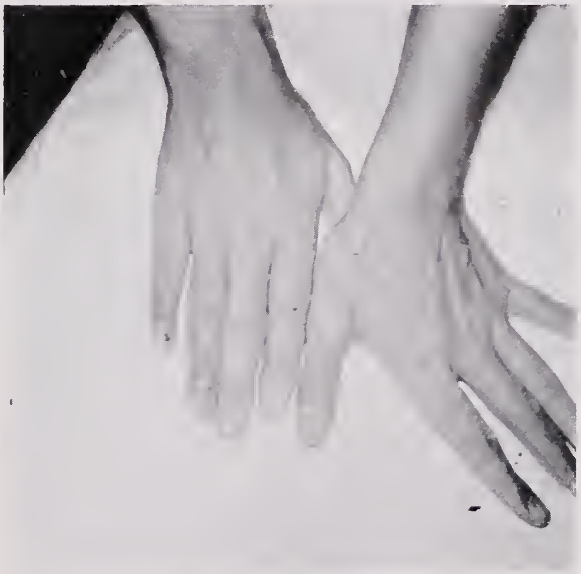

Fig. 6B—Pustular psoriasis after treatment with azaribine.

in the very best of hands often results in serious damage to such vital organs as the liver, kidneys, the gastrointestinal tract, and the hematopoietic system; and in some cases death.

Because plaques of psoriatic skin contain cells which proliferate rapidly, they are, like cancer cells, quite responsive to antineoplastic agents.

Three drugs, all antimetabolic agents, have been reported effective in producing remissions in patients with severe recalcitrant disease; Methotrexate, a folic acid antagonist; Azaribine, an orotidylate decarboxylase inhibitor, and Hydroxyurea.[5-7] Methotrexate has been approved for use in severe recalcitrant psoriasis by the Food and Drug Administration. Azaribine has been approved for use as an investigational agent in severe psoriatic disease and is soon to be released for general use. To date, Hydroxyurea has not been approved even for limited investigational use, therefore, its use in psoriasis will not be discussed. Mycophenolic Acid is a fourth agent which appears promising for systemic treatment of psoriasis. Early clinical trials of this drug have recently begun.[8]

Methotrexate. Several dosage schedules have been used in the treatment of psoriasis. Those most commonly used are: (1) a course of 2.5 mg daily for five to seven days with an interval of three to five days between courses; (2) 25 to 50 mg taken as a single oral dose once weekly; (3) 25 to 50 mg given as a parenteral dose once weekly, and (4) 2.5 to 15 mg given orally in three to four divided doses over a 24 to 36 hour period. Each dosage regimen has its advantages and disadvantages. Based on the knowledge that the cytotoxicity of a drug, particularly methotrexate, is dependent on the length of time that drug remains in contact with normal cells, and based on preliminary study of liver abnormalities associated with methotrexate treatment of psoriasis, the single dosage regimens, oral or parenteral, appear to offer less toxicity. All patients considered candidates for treatment with methotrexate should have thorough assessment of liver and kidney function and the status of the hematopoietic system before drug therapy is instituted. A liver biopsy is suggested in all patients prior to starting treatment. Except in

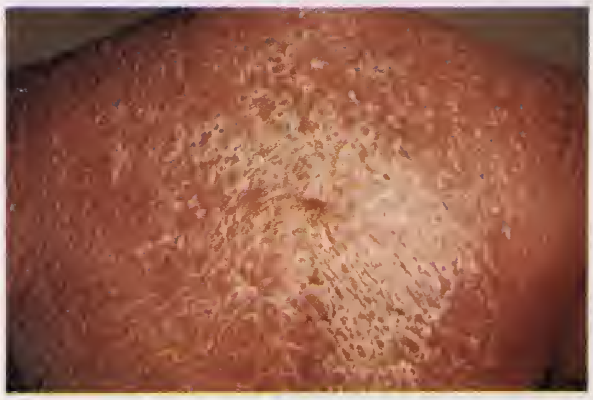
Fig. 7A—Erythrodermic psoriasis before treatment with azaribine.

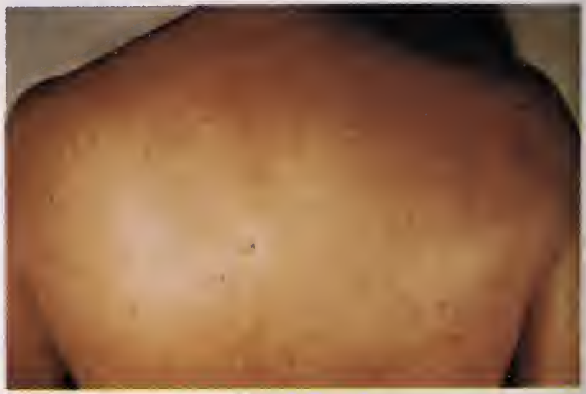
Fig. 7B—Erythrodermic psoriasis after treatment with azaribine.

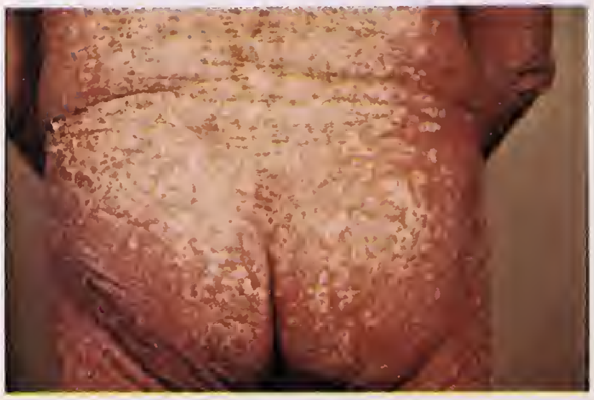
Fig. 7C—Erythrodermic psoriasis before treatment with azaribine.

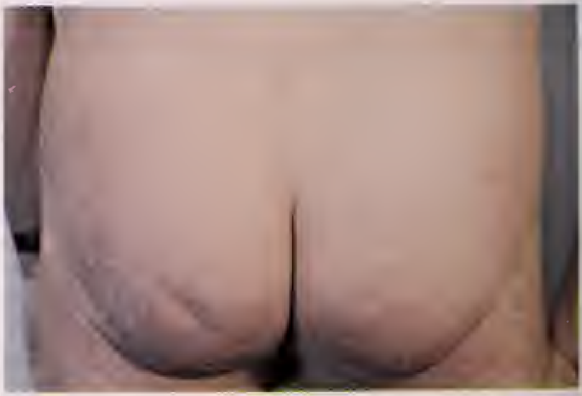
Fig. 7D—Erythrodermic psoriasis after treatment with azaribine.

rare instances patients with liver diseases are NOT candidates for treatment. Poor renal function calls for lower drug dosages. Methotrexate should not be administered in patients with low white blood cell and/or low platelet counts. Once treatment with methotrexate has been initiated a white blood cell count and a platelet count should be obtained prior to the administration of each dose or course of drug; again, low platelet and/or white cell counts are *contraindications to drug administration.* Hepatic and renal studies should be performed at least quarterly. Liver biopsy is thought to be indicated once every six to twelve months in patients demonstrating liver abnormalities prior to treatment and who are on continuous therapy. Treatment programs for each patient must be individualized; some may require treatment weekly to maintain a remission, others may require treatment monthly. Complete clearing of disease should not be the end point, or goal of treatment. Rather, the goal should be clearing sufficient to maintain patient comfort and a functional state of being. Attempts should be made, whenever possible, to interrupt treatment for prolonged periods of time.

Adverse reactions known to occur with methotrexate include those related to the central nervous system, as nausea, malaise, fever, dizziness; the gastrointestinal tract, nausea, vomiting, diarrhea, ulcerative stomatitis, gastrointestinal bleeding; hematopoietic system, low white cell, platelet and red cell counts, and in other organs and systems, pulmonary infiltrates, hepatic and renal injury, and in a small number of patients, death. Hepatic injury appears to be related to obesity, alcoholism and diabetes. Elderly patients, even those in whom all pretreatment indices are normal, appear to tolerate methotrexate poorly, therefore, lower doses and very careful observation are required in this group of patients. Because methotrexate is capable of causing an exaggerated sunburn effect in the presence of ultraviolet light, it should not be used in conjunction with ultraviolet light exposure. Methotrexate may cause abortions and fetal malformations, therefore, its use is contraindicated in females of childbearing age unless some reliable form of contraceptive is used.

Azaribine. In an effort to find an effective, safer antimetabolic agent for recalcitrant psoriasis, several limited but well controlled studies were begun with the pyrimidine antagonist, triacetyl-6-azauridine (azaribine). This drug has been found effective in causing complete remissions in over 75 percent of patients treated to date. In one study 21 of 51 patients treated successfully had been previously found to be refractory to methotrexate, or had experienced difficulty in tolerating the drug. In this same study only two patients were found to be refractory to treatment with azaribine; azaribine blood level determinations in one patient implicated a defect in drug absorption. In the other patient, who had previously maintained a disease-free state for ten months on continuous azaribine therapy, a second course of drug, after a drug-free period, was not accompanied by a disease response in spite of adequate absorption. Approximately 40 patients have been maintained successfully on continuous azaribine, without adverse effects, for periods ranging from 18 months to six years.

Drug dosages of azaribine normally used to initiate treatment range from 125 to 200 mg/kg per day administered in three divided doses. Once a remission is induced or the red cell count approaches the lower limits of normal, the drug dosage is reduced by one-half or more. The dosage at this stage is individualized until clearing is maximal. Some patients require drug only one day out of three, others require up to 200 mg per day for maintenance of remissions. Induction of remissions normally takes from three to six weeks. Once a remission is induced it is best to terminate drug therapy and reinstitute it, as required, during exacerbations. Most patients may be maintained in remission by using topical preparations on a regular basis.

A very significant advantage to the use of azaribine is its favorable therapeutic index and limited number of adverse drug effects. Most of these effects are detected during the first two or three weeks of therapy. Nearly all patients will experience a reduced hemoglobin and red cell count during high-dose therapy. Both return to pretreatment levels on low-dose or maintenance therapy. Since this change in hemoglobin and red cell mass occurs over a prolonged period of time, most azaribine treated patients will not experience the usual signs and symptoms of anemia. Therefore, close attention must be paid to red cell values until a dosage of drug is titrated which will maintain a disease response, but does not inhibit the hematopoietic system. White cell and platelet counts are, except in very unusual circumstances, not affected by azaribine.

Probably the most serious adverse effect experienced to date with azaribine is related to the central nervous system. In approximately 10 percent of patients these effects are manifested as expressive aphasias, somnolence, hyperreflexia, asterixis, myoclonia, visual aberations, and in cases not properly monitored, coma. All of these manifestations are reversible upon withdrawal of the drug.

Some patients complain of nausea, others increased appetite, and a very few, diarrhea.

To date no other adverse effects have been documented as being related to the administration of azaribine. However, it is recommended that prior to the administration of azaribine each patient should have complete examination of the hematopoietic system, renal function, liver function, and an electroencephalogram. Abnormalities in these organs or systems do not contraindicate the administration of drug, but may give the therapist a feel for the proper dosage to be instituted. At present, it is also recommended that patients having a previous history of occlusive vascular disease be excluded from treatment. A complete blood count is obtained every three days during high-dosage therapy, and on each subsequent office visit during low-dose therapy. Liver and renal function studies are obtained once each eight to twelve weeks.

Again, it is necessary to stress that because of the potential hazards of using antineoplastic agents, *their use must be limited to patients with severe, recalcitrant, and disabling psoriasis and/or arthritis, and by persons thoroughly knowledgeable and experienced in their pharmacology, toxicology and use.*

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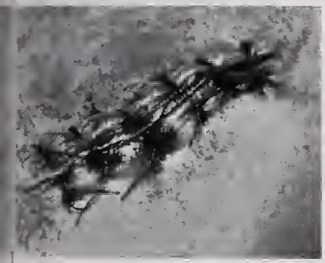

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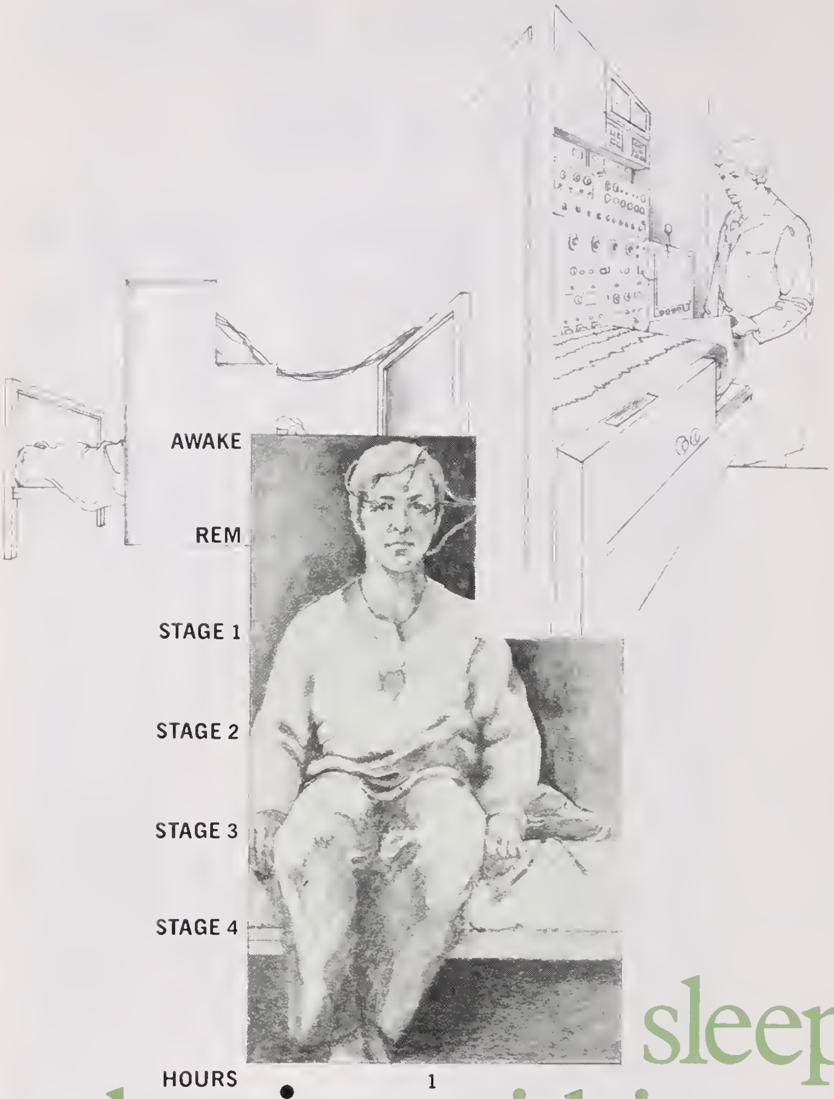

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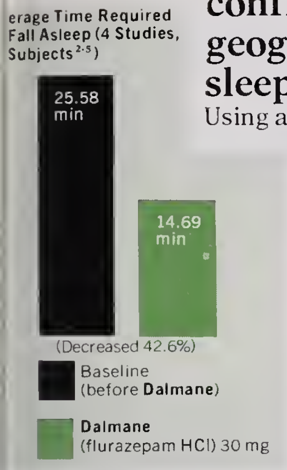

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C traindications: Known hypersensitivity to flurazepam HCl.
W nings: Caution patients about possible combined effects with alcohol and other CNS d ressants. Caution against hazardous occupations requiring complete mental alertness ., operating machinery, driving). Use in women who are or may become pregnant only when p ential benefits have been weighed against possible hazards. Not recommended for use in p sons under 15 years of age. Though physical and psychological dependence have not been orted on recommended doses, use caution in administering to a iction-prone individuals or those who might increase dosage.
P cautions: In elderly and debilitated, initial dosage should be ited to 15 mg to preclude oversedation, dizziness and/or ataxia. I ombined with other drugs having hypnotic or CNS-depressant e cts, consider potential additive effects. Employ usual precautions atients who are severely depressed, or with latent depression or s cidal tendencies. Periodic blood counts and liver and kidney ction tests are advised during repeated therapy. Observe usual p cautions in presence of impaired renal or hepatic function.
A erse Reactions: Dizziness, drowsiness, lightheadedness, s ggering, ataxia and falling have occurred, particularly in elderly o lebilitated patients. Severe sedation, lethargy, disorientation and c na, probably indicative of drug intolerance or overdosage, have b n reported. Also reported were headache, heartburn, upset s nach, nausea, vomiting, diarrhea, constipation, GI pain, nervous-n s, talkativeness, apprehension, irritability, weakness, palpitations, c st pains, body and joint pains and GU complaints. There have a been rare occurrences of sweating, flushes, difficulty in focusing, rred vision, burning eyes, faintness, hypotension, shortness of ath, pruritus, skin rash, dry mouth, bitter taste, excessive saliva-, anorexia, euphoria, depression, slurred speech, confusion, lessness, hallucinations, and elevated SGOT, SGPT, total and d ect bilirubins and alkaline phosphatase. Paradoxical reactions, , excitement, stimulation and hyperactivity, have also been orted in rare instances.
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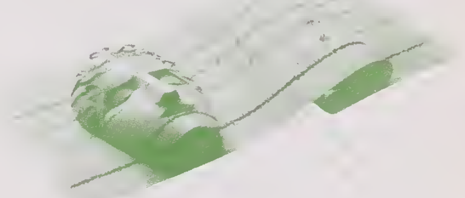

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Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, descreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

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*E.D. Freis: The Modern Management of Hypertension, V.A. Information Bulletin, 11-35.

TO KEEP BLOOD PRESSURE DOWN AND KEEP POTASSIUM LEVELS UP

The Eczemas

ROBERT W. GOLTZ, M.D.*

This paper reviews the most important kinds of dermatitis and eczema. They include atopic dermatitis, primary irritant and allergic contact dermatitis, eczematous rashes produced by infectious agents, and several eczemas of unknown etiology, including seborrheic, dysidrotic and nummular types. Together, they constitute a large percentage of all disorders of the skin encountered in clinical practice.

THE TERM "ECZEMA" HAS long been used to describe one type of acute inflammatory process in skin. It is characterized by vasodilation which leads to redness, and edema which produces diffuse swelling, or when superficial, blistering, exudation ("weeping") and crusting. These are the signs of acute dermatitis, and in fact the terms dermatitis and eczema have come to be used interchangeably. Many skin lesions may be said to be eczematous or have been eczematized when they become acutely inflammed. Thus, the term eczema may be applied to cutaneous inflammation having many different causes. It is better to think of a group of "eczemas," rather than "eczema" as a single entity.

While "eczema" derives from the Greek word "to bubble," and thus referred originally to acute exudative dermatitis, in clinical practice the term is also used for chronic dermatitis. The chronic eczemas show the signs of prolonged inflammation of the skin; leathery rather than edematous skin thickening, lichenification, pigmentary changes, hyperkeratosis and scaling, and usually, excoriation with resulting scarring.

This is the clinical appearance of all eczematous skin diseases, whatever their cause. The specific kinds of eczema include atopic, contact, seborrheic, and the infectious eczemas (fungal, bacterial or mixed). There are clinically distinctive kinds of eczema such as nummular eczema, which are poorly understood but seem to overlap with several of the above. Finally, there is a phenomenon of eczematization arising in a number of other skin diseases—psoriasis, lichen planus, or around lesions of molluscum contagiosum, to choose a few.

Atopic Eczema

Atopic eczema is the form which appears to be genetically determined and bears some relationship to the other atopic disorders—hayfever and allergic asthma. There is evidence that it is in some way related to imbalance of the immune mechanisms—either hyperreactivity or immunological deficiency, or likely a combination of both. Patients with atopic eczema also have other anatomical and functional peculiarities, including dryness of the skin ("ichthyosis vulgaris") and unusual responses to pharmacological agents. The intense pruritus is also a distinctive feature, as are the resulting excoriation, lichenification, and hyper- and hypopigmentation of the affected areas.

Clinically, atopic eczema usually begins in infancy or early childhood, with a tendency to become much worse at puberty. Typical areas of involvement are the face, neck, upper trunk, cubital and popliteal fossae, hands and wrists. When these areas are involved, there is little difficulty in making the diagnosis, even at a glance. When the eruption is less extensive or involves unusual areas, such as the hands alone, the correct diagnosis is less obvious and even experienced dermatologists may differ as to whether a certain case should be labelled atopic.

Because of its chronicity and lack of a clearly identifiable cause, management of atopic eczema is particularly difficult. "Allergic" management, consisting of skin tests and dietary eliminations, is disappointing. Topical therapy, with application of bland wet dressings and steroid ointment, is the only available treatment in most cases. Irritants like wool and dust, which provoke spells of itching, should be avoided. Hydration of the too-dry skin by daily bathing in water (without soap or detergent), followed by application of bland oils is helpful. At present, systemic therapy has little to offer. Systemic corticosteroids should be used only rarely, for control of especially severe acute flareups. These are often better treated by a few days of bed rest with wet dressing, rather than putting the patient on sys-

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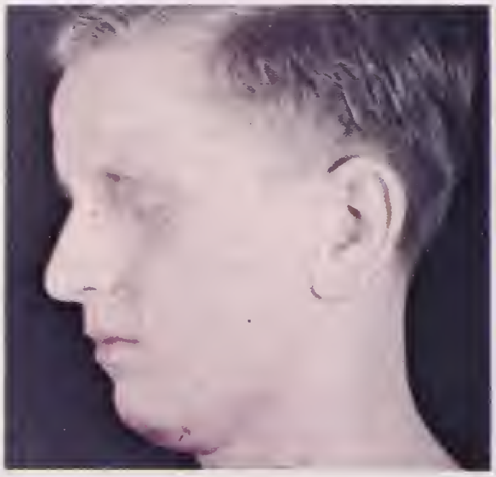

Fig. 1—Atopic eczema. The patient demonstrates redness, scaling and thickening of the skin and numerous excoriations as evidence of intense pruritus.

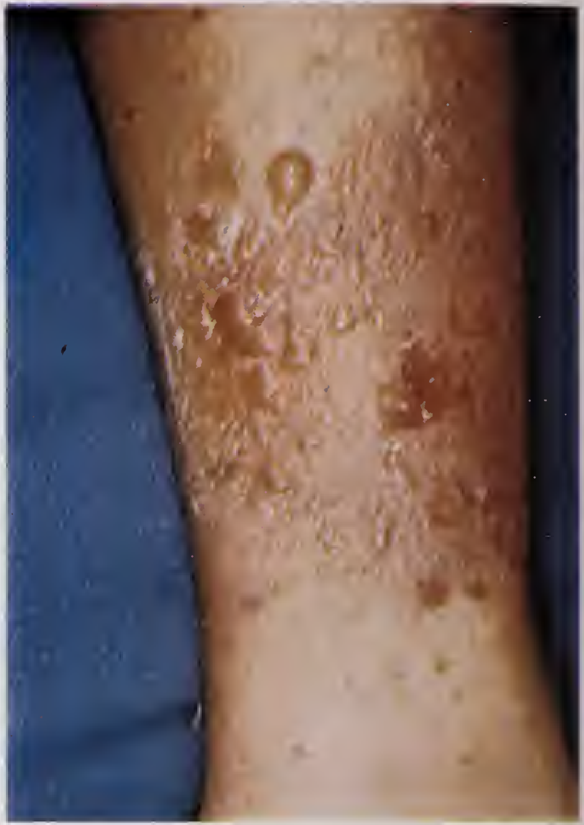

Fig. 3—Acute allergic contact dermatitis to poison ivy. The large vesicles are typical of plant dermatitis.

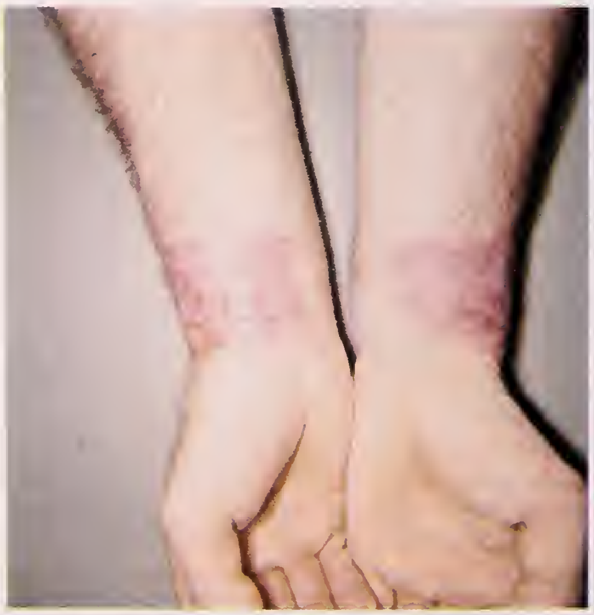

Fig. 2—Allergic contact dermatitis from ingredients of leather wrist bands.

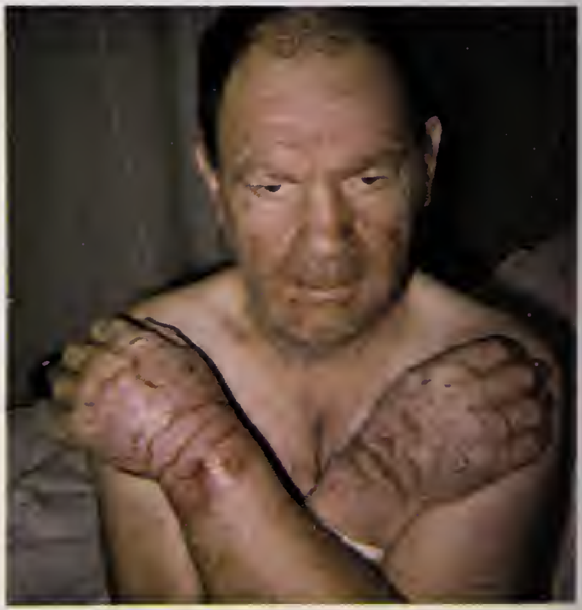

Fig. 4—Photocontact dermatitis. Eruption largely limited to the exposed areas of skin.

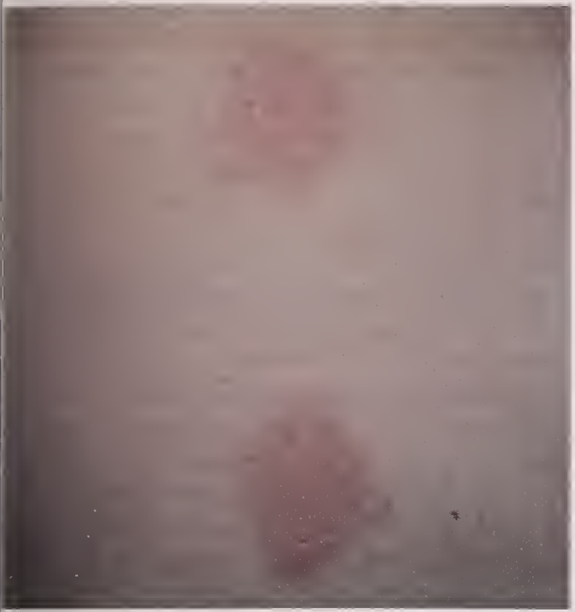

Fig. 5—Positive patch tests to benzalkonium contained in eyedrops as a preservative.

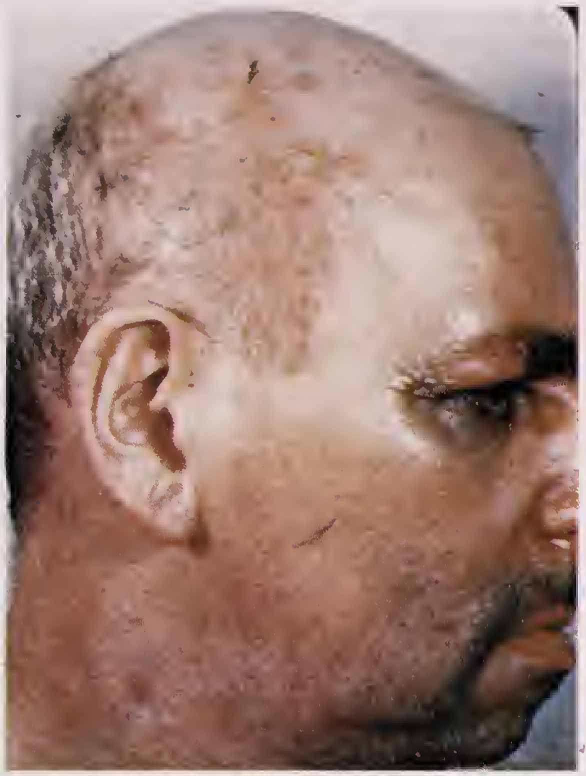

Fig. 6—Seborrheic eczema.

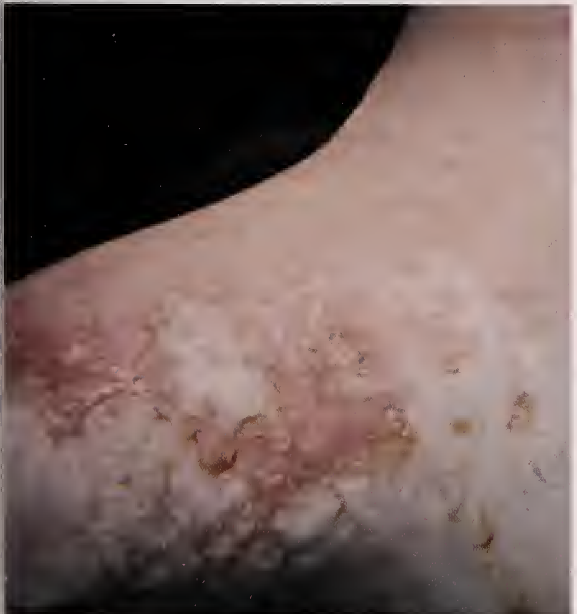

Fig. 7—Infectious eczematoid dermatitis.

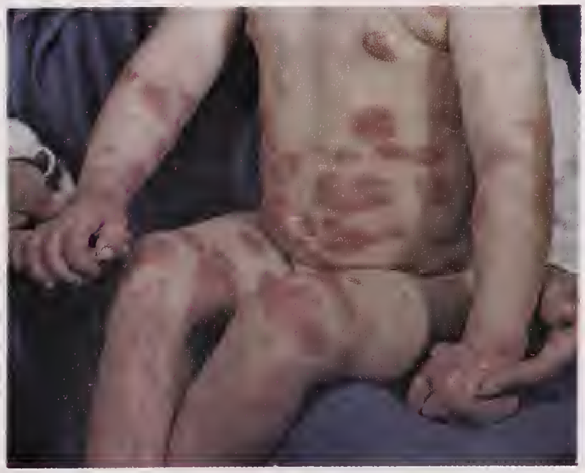

Fig. 8—Nummular eczema in an atopic child.

temic corticosteroids, which may be difficult to withdraw. Other systemic agents, including antihistamines, sedatives or tranquilizers, and so-called antipruritic drugs, are of limited value. Patients and their parents need to understand that, as in asthma, there is at this time no "cure" for atopic eczema and that the aim of treatment is to keep the disorder under the best possible control. This requires continuing surveillance, resourcefulness, and patience on the part of both patient and doctor.

Contact Eczema

Successful management of contact dermatitis constitutes one of the most challenging yet rewarding opportunities for physicians responsible for care of patients with skin disease. Generally, successful therapy centers on identification and removal of the cause, together with proper treatment of the damaged skin while avoiding further injury to it.

Contact dermatitis may be caused by either primary irritants or by allergens. Primary irritant dermatitis is by far the more common. A good history will usually uncover the cause; patients themselves often know what they have touched that has irritated their skin. In occupational contact dermatitis, a number of workers exposed to the same irritant are likely to be affected. In these cases, a visit by the physician to the factory itself may be most important. Primary irritant dermatitis will be confined to skin areas contacted by the offending chemical, unless secondary bacterial infection or allergic contact dermatitis, caused by application of salves containing cutaneous sensitizers, has complicated the clinical picture.

Allergic dermatitis may be produced by a wide variety of contactants. Some of these, like the oily resin of poison ivy/poison oak, will produce an allergic reaction in almost everyone, while other substances are weak sensitizers, and will produce contact dermatitis in only a few. Unlike primary irritants, contact allergens do not produce dermatitis on the first exposure. Usually a number of exposures are needed to initiate the immunological events leading to a sensitization reaction, and even after the sensitizing exposure an incubation period of 7-10 days is required. On subsequent exposure of already sensitized skin, no such incubation period is necessary, and the dermatitis usually appears within a few hours. A few allergens, notably neomycin, require longer time for the reaction to occur—even to a week. This is important to keep in mi in interpreting patch tests to these substances.

Allergic contact dermatitis first appears at t site of greatest exposure, and almost always most severe there. Unlike primary irritant de matitis however, the allergic type may spread involve contiguous skin areas, and in a few cas disseminates over the body, perhaps becomi generalized. Identification of the cause depen on careful history taking, followed by patch te ing with suspected contactants. Care should taken that substances applied as patch tests sufficiently dilute to avoid a primary irritant rea tion. Appropriate concentrations for patch testi can be found in tables in a number of textbooks

A special form is photocontact dermatitis, which application of a photosensitizing chemic plus exposure to light, is necessary to produce reaction. Naturally the photocontact dermatit appears first and most severely on light expos areas, such as the head and neck, hands ar forearms, although it may not remain limited these areas. Photocontact dermatitis due to plan like meadowgrass appears on sites of exposure the offending plant—often the legs or thigh Photosensitizers appear as bacteriocides in number of "medicated" soaps, shampoos and co metics, and as essential oils in scents and pe fumes. The resulting photoallergic reaction wil of course, appear at the sites of application those cosmetic agents and perfumes. It shoul be remembered that their use is no longer co fined to the female sex, since men also no use scented shaving lotions or other toiletri which may contain these agents.

A special technique known as photopatch tes ing is required for positive identification of the agents. This consists of application of suspecte materials for 48 hours under a light-tight cove followed by measured exposure to the sun c other source of ultraviolet and visible light. Onl then will the typical eczematous reaction appea

For permanent cure of contact or photoconta dermatitis, it is necessary to avoid the offendin substance after it has been identified by histor or patch testing. Avoidance may involve wea ing of special clothing or shoes, even a change c occupation. Medical treatment, while it ma produce temporary improvement, is seldom abl to produce a lasting cure.

Treatment of contact eczema consists of application of soothing and cleansing wet dressings, nd mild topical remedies. Care should be taken o avoid those agents which may in themselves produce contact sensitivity in an already damaged nd inflammed skin. These include such common remedies as neomycin, vioform, furacin, enzocaine or nupercaine, and creams or lotions ontaining preservatives like the parabens, merurials or ethylenediamine. In general, the ewer fluorinated topical corticosteroids are the most rapidly effective, but it should be remembered that the time-honored 1% hydrocortisone ointment or cream is often sufficient, at considerably lower cost.

Systemic corticosteroid therapy, while not to be elied on to suppress chronic contact dermatitis vhen the cause has not been identified, may be helpful in acute cases. In selected cases, such as acute poison ivy dermatitis, a one to two week ourse of prednisone may greatly accelerate healing and contribute much to the patient's comfort.

Seborrheic Eczema

Seborrheic eczema gets its name from its predilection for those areas of skin rich in sebaceous glands; the scalp, ear canals, sides of the nose, central chest and back. We know nothing of its cause, and little more about its cure. There are some theoretical grounds, but little scientific evidence, to suggest that infection with bacteria, pityrosporon ovale or demodectic mites may play at least a secondary role in seborrheic dermatitis. Perhaps these organisms thrive on the oily sebum. Many believe that seborrheic dermatitis is an nflammatory and more severe phase of ordinary dandruff. Supporting the at least partial role of organisms in its cause is the usual response of seborrheic dermatitis to bacteriostatic agents such as vioform and sodium sulfacetamide (Sebizon otion®—Schering). However, topical and systemic antibiotics seldom help. Topical corticosteroids preparations, while beneficial because of their antiinflammatory action, are rarely curative. Systemic corticosteroids are seldom needed, except briefly in extremely severe, widely disseminated cases. The time-honored remedies for seborrheic dermatitis, sulfur and salicylic acid, probably produce their effect by altering the keratin in which the organisms grow.

Infectious Eczemas

Bacterial Eczemas

We have already mentioned that the denuded skin of patients with contact, atopic or seborrheic dermatitis, coated with serous exudate, and stripped of much of its normal keratinous barrier, is likely to become secondarily invaded by bacteria. The resulting infection makes the dermatitis more severe and extensive and purulent discharge may change the clinical appearance. In a few cases, bacterial infection is the primary event. For example, around a chronic skin ulcer or infected laceration may appear an eczematous dermatitis, usually covered by a purulent crust, and extending out for several centimeters. This is called infectious eczematoid dermatitis. Not surprisingly, it responds well to treatment with antibiotics. The organisms are usually gram positive staphylococci and streptococci, and systemic penicillin or erythromycin are the drugs of choice. While it is tempting to use antibiotics or antiseptics locally as well, they are usually best avoided, since contact sensitivity to neomycin, furacin or vioform may delay healing of the eczema. By removing the serous-purulent crusts which harbor bacteria, wet dressings are helpful, and this is one form of eczema where gentle soap and water cleansing is indicated. Perhaps surprisingly in the face of overt infection, topical corticosteroids are also helpful. They restore the normal antibacterial defenses of the skin through reversal of the inflammatory reaction, reduction of edema, and lessening of the serous exudate on the surface.

Eczema Due to Fungi and Yeasts

Infection of the skin with dermatophytes may produce an inflammatory dermatitis which meets the morphological criteria of eczema. On the legs and feet of American troops subjected to prolonged exposure to warm water in rice paddies in Vietnam, mixed infections with fungi and bacteria produced a most disabling and stubborn eczematoid inflammation.

Treatment of superficial fungal infections depends on eradication of the responsible organisms, as well as the usual antiinflammatory remedies. Since fungi thrive on a moist environment, prolonged wet dressings are usually not advisable, although in the presence of marked secondary bacterial infection, removal of crusts by potassium permanganate compresses may be useful, at least at first.

Oral griseofulvin in doses of 1 gm./day is usually needed. Effective topical fungicides include Tinactin®, Haloprogin®, or Miconazole®. The traditional Whitfield's ointment, which contains salicylic and benzoic acid, is helpful by removing the outer layers of keratin in which the dermatophytes proliferate. Secondary bacterial infection, including the not infrequent ascending lymphangitis and lymphadenitis, should be treated by penicillin or erythromycin. Bed rest, with elevation of the extremity is usually advisable in the face of significant bacterial infection.

Yeast Infections

Eczematous reactions to skin infection with Candida albicans are usually confined to moist, intertriginous areas such as the inguinal and intergluteal folds, under the breasts or fat rolls of the obese, or the corners of the mouth. In hot and humid summer weather widespread candidal dermatitis occurs on the back of bedridden patients. Candidal lesions are erosive rather than scaly, and there may be considerable exudation of a milky fluid. Small vesicopustules at the spreading edge of the patches are the clinical signs most helpful in the diagnosis of candidiasis. Laboratory confirmation is easily made by identification of budding yeast forms and pseudohyphae in smears of the curdy exudate scraped from the surface of the plaques.

Since candidiasis is a frequent complication of immunosuppression or endocrine disease, particularly diabetes mellitus, these should be ruled out in extensive or resistant cases. A search for a source of chronic reinfection, as in the mouth, gastrointestinal tract or vagina, should also be made. In resistant anogenital yeast infections, reinfection from the sexual partner should be kept in mind.

Successful management of candidiasis involves cleaning and drying of the skin, and application of lotions, creams or dusting powders containing nystatin, amphotericin or vioform. These may be used on an alternate basis, as nystatin dusting powder during the day, and 3% vioform cream at night. Haloprogin® is also an effective remedy. In the unusual cases when these more modern remedies fail, resort may be made to the messy but effective aniline dyes, 1% gentian violet, or brilliant green solution.

Dysidrotic Eczema

A considerable number of people present with stubborn patchy dermatitis of their hands and feet. Usually this involves the sides of the fingers, and patches on palms and soles. The disorder begins with crops of small vesicles which itch intensely. This is followed by scaling and erythema. No cause for this can be found, although fungus infection should be ruled out, and a search made for irritating or sensitizing contactants. Often these patients have hyperhidrosis of the hands and feet, and the disease has been considered to be a disorder of the sweating mechanism, hence the name dysidrotic eczema. Since sweating of the palms and soles is largely controlled by psychic influences dysidrotic eczema has been considered to be, at least in part, of psychosomatic origin. It must be admitted, however, that our knowledge of the real cause of dysidrotic dermatitis is woefully incomplete, and so is our ability to cope with it. Topical corticosteroid creams are helpful but not curative. Hyperhidrosis may be at least partially relieved by anticholinergic drugs such as banthine,® probanthine® or prantal.® Unfortunately, all of these have troublesome side effects which limit their usefulness.

Nummular Eczema

Nummular eczema gets its name from the fact that it occurs in scattered small coin-like patches. These are usually symmetrically distributed on the trunk and proximal extremities. These patches are extremely pruritic, and rubbing and scratching produces an edematous, raised, red, eroded patch which drains a serous or seropurulent exudate. The cause of nummular eczema is unknown, although some cases are clearly related to atopic disease. Secondary infection of the skin lesions usually plays a significant role, and antibacterial remedies usually produce improvement, although seldom complete cure. This troublesome eruption is unusually chronic and resistant to treatment. Corticosteroids, tar and vioform are the standard topical remedies.

Contact Dermatitis

Office Diagnosis and Management

WILLIAM F. SCHORR, M.D.*

Contact dermatitis is an extremely common disease which can be widespread and cause prolonged disability. Measures wherein this disability can be curtailed and limited have been outlined. The diagnostic exercises utilized in the study of contact dermatitis can be fascinating and very helpful. This involves detective work with a high yield of patient cure.

CONTACT DERMATITIS IS best described as redness and inflammation of the skin caused by chemicals to which the patient's skin has been exposed.[1] It is a frequent cause of visits to the dermatologist's office and commonly seen in the practice of family medicine.

There are two main varieties of contact dermatitis: irritant, the more common, and allergic.[1] Irritant contact dermatitis is provoked by frequent defatting of the skin by excessive moisture or damage induced by acids, alkalis, resins or chemicals which are capable of injuring any person's skin if sufficient exposure is allowed. Allergy or delayed type hypersensitivity plays no part in this mechanism and allergy testing or the common patch test has no place in its evaluation. A housewife can expect to suffer from this dermatitis on her hands occasionally. A woman in her daily chores with her hands in cleansing agents, soaps, detergents, bleaches, oven cleaners, fruit and vegetable juices, polishes, wall cleaners and diaper rinses ultimately defats the skin to a degree where a chapped phenomena ensues. With continued defatting of the skin or continued irritant exposure, erythema, edema, vesiculation, scaling and greater disability usually develops. Unless the housewife refrains from all wet work until her hands are healed, therapeutic results cannot be expected. After healing, they should go back to their housework in a modified fashion. Damaged or inflamed eczematous skin, whether it be provoked by an irritant contact dermatitis or by a stasis dermatitis, while inflamed, carries with it a higher percent chance of developing delayed type hypersensitivity or true allergy. It is a common practice for the woman with housewive's eczema on her hands to realize that the housework is playing some role in the causation of her inflamed skin, and on her own she usually resorts to the use of rubber gloves. While this would appear to be an answer, in practice it is not always true. The rubber gloves, even if they are lined, when used on inflamed skin cause maceration and sweating and provoke a further irritant response. Recognizing the fact that damaged or inflamed skin while it is inflamed carries with it a greater chance of developing true allergy, this patient now with the rubber gloves on her inflamed hands is more apt to become allergic to chemicals used to manufacture rubber. If this happens, the patient may not only have a severe flare of her hand eczema but may then develop a dermatitis elsewhere on her body. The woman who becomes allergic to rubber would naturally be expected to show a dermatitic response where the elastic of her bra, her girdle, her panties or the rubber glues in her shoes come in contact with the skin and the problem is compounded.

The worker in industry who handles solvents, oils, greases, acids or alkalis, like the housewife, falls victim to irritant contact dermatitis on his hands (Figure 1) and at times elsewhere on the body. If this worker is not removed from his job for at least several weeks until the skin is healed, he, like the housewife, carries a greater risk of developing an allergic response to chemicals in his work. Should the chemical be one commonly used in many areas of our environment, chronic disability can result. This disability can often be avoided if the patient discontinues exposure until the skin is completely healed. Treatment includes contact isolation, removal of all possible offending chemicals and application of medication with little sensitizing potential. Healing usually results within a few weeks.

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*Marshfield Clinic and Marshfield Clinic Foundation for Medical Research and Education, Marshfield, Wisconsin.

Allergic Contact Dermatitis

Allergic contact dermatitis, unlike irritant contact dermatitis, can occur only in sensitized individuals. Our daily human exposure to chemicals in our environment reflects many thousands of chemicals. There are better than 5,000 chemicals that can be used just to make any one perfumed item we meet in our everyday life. Modern day industry utilizes a very large number of chemicals and obviously, it is not possible to do allergy tests to each chemical in one's environment. It becomes necessary to recognize clinical clues and to evaluate important points in the patient's clinical history. It also becomes imperative that we understand and recognize the concept of the sensitization indices of chemicals. In the sensitization index we reflect chemical A's much greater ability to produce allergy in a given population than chemical B. Chemical A may have the capacity of causing allergy in 5% to 10% of the population whereas chemical B may be capable of causing or inducing allergic disease in less than 0.01% of the population. The greater the sensitization index, the higher risk factor we have in industrial medicine and the higher the sensitization index, the greater the risk we realize in terms of the various medications prescribed either by the physician or used by the patient without the physician's prescription. It is important that we utilize medications which carry with them the least possible sensitization index.

In 1972 the North American Contact Dermatitis Research Group studied 1,200 patients in the United States and Canada who clinically had a diagnosis of contact dermatitis, cause unknown.[2] This study describes not only the relative frequency of allergy and the risk factors of the most common allergenic chemicals in America today, but it also guides the physician so that he might obtain these allergens and utilize them correctly in his daily office practice. When positive patch tests to these allergens are found, this reference can guide the physician in advising the patient how to avoid the many sources of possible exposure to the particular chemical the patient is allergic to. In this way complete and final cure can be obtained.

Nickel Sulfate

In 1972 the most common cause of allergic skin disease in North America was nickel sulfate. Eleven percent of 1,200 patients with contact dermatitis were allergic to nickel. Most of the patients allergic to nickel are young women who sometime in the past had their ears pierced and this damaged skin subsequently developed true hypersensitivity to nickel. Initially, the dermatitis begins about the ear lobes (Figure 2). With the passage of time, however, the patient will return to the physician's office with a band of dermatitis around the wrist from a watch or a piece of jewelry or a band of dermatitis around the neck from a necklace or dermatitis under a bra clip, a metal buckle or other source of nickel exposure.

Potassium Dichromate

Another common cause of allergic skin disease is potassium dichromate. We test for potassium dichromate sensitivity with a 0.5% solution. Eight percent of all patients with contact dermatitis seen by these 13 dermatologists[2] had allergic reactions to hexavalent chromium or potassium dichromate. Potassium dichromate is another chemical which has widespread usage in our environment. While it is true that chromate allergy can occur from costume jewelry in the female population, it is more commonly seen as a severe and serious cause of disability in the worker in industry. Exposure to chromate occurs in many occupations. Leather products, bleaches, galvanized iron, tanning agents, furs, photography, photoengraving, lithography, electroplating, yellow and orange paints, ink manufacture, stainless steel, chrome plating, diesel engine fluids, welding, cement, linoleum, glass, chromate impregnated wood, decorating porcelain, fireworks, wax, waterproofing fabrics, rust inhibitors, antifreezes, automobile greases, caulking compound, cooling system additives (auto, truck and diesel) and cutting oils are all sources of chromate exposure.[3] There are many industrial sources of exposure to hexavalent chromium and unless the diagnosis is made, the patient finds no relief. Almost all American shoe leather is tanned with hexavalent chromate and the chromate allergic patient may have to use costly custom made vegetable tanned shoes the rest of his life or continually suffer from a chronic severe dermatitis of his feet (Figure 3).

Paraphenylenediamine

Paraphenylenediamine is another of the most common causes of allergic skin diseases in the United States. To make this diagnosis a 48 hour patch test is performed to 1% paraphenylenediamine in petrolatum. Once identified as the cause of disease, the patient is instructed in the many sources of exposure. Paraphenylenediamine is widely used by women to dye their hair. It may be found in clothing and in shoes. Para-amino type compounds such as paraphenylenediamine have wide use on an industrial basis in this country and abroad. The patient allergic to paraphenylenediamine will not only break out from the hair dye, the clothes, the shoes or other such everyday exposure but will also have a recall of their skin disease by exposure to chemicals which are structurally or chemically similar to paraphenylenediamine. The body is not able to tell the chemicals apart and we have a phenomenon of cross-sensitivity. Therapeutic agents such as benzocaine, the sulfonamides, carbutamide, paraaminosalicylic acid and HydroDIURIL can all cause an outbreak of dermatitis in the patient allergic to paraphenylenediamine.[3] Paraphenylenediamine is an industrial exposure risk for hair dressers, furriers, leather processors, rubber vulcanizers, rubber plant workers, printers, lithographers and x-ray technicians to mention only a few. If this diagnosis is properly made and all sources of exposure to paraphenylenediamine or closely related chemical compounds can be eliminated, cure can be expected. Short of this diagnosis and appropriate patient guidance, recurrent and recalcitrant disease results.

Potential Sensitizers

Known potential sensitizers such as neomycin sulfate, ethylenediamine, Benzocaine, thimerosal, ammoniated mercury, wool wax alcohol, paraben mixture, dibucaine, cyclomethycaine sulfate and turpentine are all found in medications used by the patient and applied to the skin. Many of them are found in other sources of environmental exposure and those that have industrial usage over and above their application in topical dermatologic remedies carry with them the greatest chance of producing widespread recalcitrant skin disease.

Ethylenediamine which showed 7% reactivity or allergic response when tested on the 1,200 patients studied is a chemical worthy of considerable attention. Ethylenediamine[2-4] is one of the most potent allergenic chemicals found in the United States today. It is widely prescribed and used in Mycolog Cream as a stabilizer. Mycolog Cream when applied to damaged or inflamed skin such as stasis dermatitis, housewive's eczema of the hands or other form of dermatitic response will with great frequency produce an added allergic event. In addition to ethylenediamine, neomycin and parabens are also found in Mycolog Cream. Neomycin[2] patch test reactivity was seen in 6% of the patients studied in 1972. It is for these reasons that most practicing dermatologists do not prescribe Mycolog Cream.

Let us take a look at the plight of the patient who has become allergic to ethylenediamine in Mycolog Cream or in other sources of exposure. If this patient needs gainful employment, ethylenediamine exposure in the following industries will preclude his employment in the manufacture of dyes, fungicides, insecticides, resins, oils, inhibitors, rubber manufacture, synthetic waxes, asphalt wetting agents, shellac solutions, lubricants, analytical chemistry, cleaners (engine, toilet bowl, metal), deodorizers, cutting oils and liquid soaps.[4] Ethylenediamine is used in the manufacturing process of all these items. Ethylenediamine is not only found in Mycolog Cream but it is also found in aminophylline and theophylline suppositories. Patients allergic to ethylenediamine may develop dermatitis when they are exposed to chemicals with a similar structural formula, allowing for the phenomenon of cross-sensitivity. Ethylenediamine allergic patients may, therefore, break out in a dermatitis if exposed to promethazine cream (Phenergan), tripelennamine cream (Pyribenzamine) and antazoline (Antistine Ophthalmic Solution).[3]

Benzocaine[5] has always been a common cause of allergic reactions and benzocaine-containing proprietary salves are widely sold, widely used and applied to stasis dermatitis or the housewife's eczematous hands. Needless to say, the dermatologist would not prescribe a benzocaine-containing topical preparation as the sensitization index would be considered prohibitive.

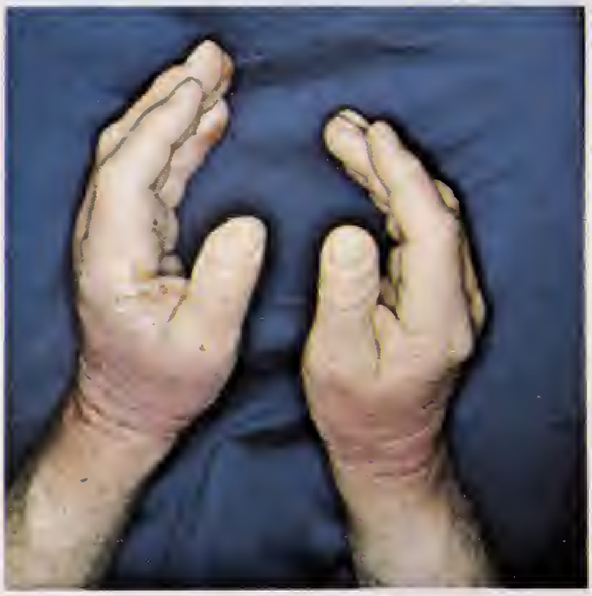

Fig. 1—Erythema, scaling, edema and fissures produced by solvents, cleansers, greases and oils on a worker's hands. This is irritant contact dermatitis.

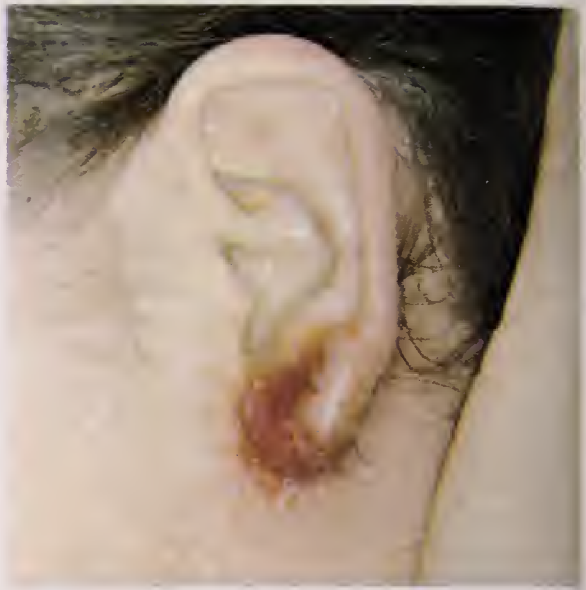

Fig. 2—Nickel allergy subsequent to ear piercing. All nickel containing costume jewelry will have to be avoided by this patient.

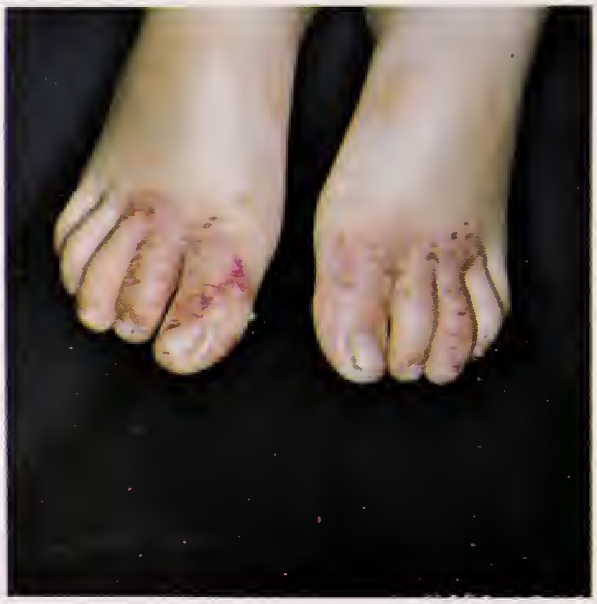

Fig. 3—Shoe allergy causes a symmetrical dermatitis of both feet. The marked symmetry is very helpful in making a clinical diagnosis. This picture could be produced by chromate allergy in the leather or by rubber glue allergy.

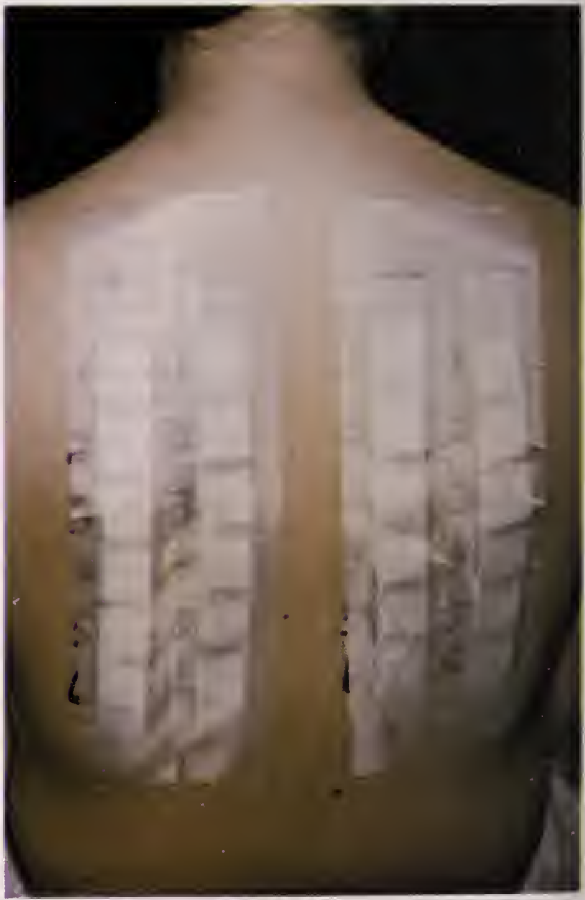

Fig. 4—Patch tests properly applied conforming to international standards.

Wool wax alcohol with its 3% incidence of allergic responses is a measure of lanolin allergy in this country. Lanolins are used widely in proprietary and everyday topical medications.[6] Lanolins are also used widely in cosmetics. Our modern day lip gloss and eye gloss cosmetics with their wet, shiny appearance on the lady's lips and eyelids are all made from lanolin fractions.[7] Lanolin (wool fat, wool grease, wool wax) is a natural product obtained from the fleece of sheep and its chemical constituents vary from time to time and place to place. In general, however, the wool wax alcohol fractions appear to be the cause of the majority of allergic responses.

Dermatitis produced by topical medications is one of the commonest causes of allergic contact dermatitis. H. J. Bandmann, et al.[5] in a study of 4,000 consecutive patients with eczema in European clinics found that 14% of all the eczemas studied were caused by therapeutic agents. While we have discussed some of the more potent sensitizers and more common offenders, ammoniated mercury and the parabens should also be considered.

Positive patch test reactions to ammoniated mercury appeared in 5% of the 1,200 patients studied by the North American Contact Dermatitis Research Group. A patient allergic to an inorganic mercurial such as ammoniated mercury may cross react with organic mercurials and the various sources of exposure to these chemicals has to be understood. Ammoniated mercury[3] is found in Unguentine Bossi, Sorsis Cream, Riasol Cream and Psoriasis Treatment Lotion by Rexall. It is also used as a depigmenting agent or a bleaching agent in the following commercially available topical preparations—Esoterica, Nadinola Bleach Cream, Peacock's Imperial Cream, Stillman's Freckle Cream, Golden Peacock Bleach Cream, Mercolized Cream and Blue Ointment. Organic mercurials are used as preservatives in cosmetics.[8] Mercurials are used rather widely in industry and again we have a chemical or a group of chemicals quite capable of causing allergic skin disease.

Paraben

In 1966[9] we reported the first case of paraben allergy in the United States and many other cases have subsequently been documented.[10-13] In the 1972 study by the North American Committee paraben allergy played a part in 3% of all allergic skin disease. The problem with paraben allergy is not one of extreme frequency in terms of disease production but one wherein the diagnosis is often not made. As we had demonstrated in our earlier publications, parabens are used in the vast majority of cosmetic and proprietary creams and lotions used by the patients. Parabens are used because they are excellent antimicrobial agents which prevent the creams and lotions from spoiling by way of bacterial or fungal growth. If we do a patch test or an allergy test to the paraben containing cream, we almost always obtain a false negative test response. We must utilize a 3% to 5% concentration of the various paraben esters, either individually or in combination, to make the diagnosis. Parabens, like neomycin, require a patch test concentraton higher than that used by the patient in order to demonstrate a true positive allergic response. This is merely a reflection of limitations within our 48 hour patch testing system. The paraben allergic patient will continue to flare as she uses a wide variety of salves and lotions all of which contain the same allergen, paraben.

In 1973[14] we documented the cross-sensitivity pattern of neomycin and this perhaps should be mentioned in view of the fact that neomycin was a factor in 6% of all allergic skin diseases in the United States. From our study and that of others[15] we see that the patient allergic to neomycin may also develop disease when exposed to gentamicin, paromomycin, kanamycin and other chemically related aminoglycoside antibiotics.

Contact History

The following points are of greatest importance in taking a dermatologic history from a patient with contact dermatitis.

1. Where and when did the skin problem begin?
2. What topical medications did the patient use?
3. What other habits or sources of chemical exposure:
   A. Home.
   B. Hobbies.
   C. Employment.
4. What household chemicals are in the patient's environment?
5. Which cosmetics does the patient use? Did the patient apply a cosmetic cream or lotion to the damaged or inflamed skin?

It is necessary to evaluate a job description of the worker. Is he exposed to formaldehyde, epoxy resins, chromates, cement acids, alkalis, solvents, moisture or excessive wetting of the skin? All of these factors must be known and only after we have this information can we make a proper diagnosis and adequately treat the patient.

Allergy Testing

Skin allergy, as we have seen, means contact dermatitis. The only test of importance in the evaluation of the average patient with contact dermatitis is the 48 hour closed patch test. Scratch tests play no part in the evaluation of allergic skin disease or allergic contact dermatitis. Scratch tests detect only immediate type hypersensitivity. It is the delayed type of hypersensitivity, however, through which allergic skin disease is mediated and produced. Dermatologic references are available which define the proper testing concentration and vehicle for each and every chemical which is known to cause any significant amount of skin disease in our environment.[2,3] While there are literally thousands of such chemicals, I would strongly advocate the usage of the North American Contact Dermatitis screening test tray which is currently available to the practicing dermatologist. This test tray is designed as a quick diagnostic screen for the physician's office and is something that can be applied by the average physician's nurse. This test tray will be re-evaluated by the North American Contact Dermatitis Research Group every six months so that the allergens will continue to maintain current relevance to our society. The publications of the North American Contact Dermatitis Research Group are available and help guide the physician in the many sources of exposure of each of these chemicals. If the physician is going to use this testing system, there are certain rules that have to be followed. He must realize that allergy tests or patch tests must not be applied while the patient has active dermatitis. He must first withdraw this patient from all chemical exposure, heal the skin and then have the patient return for proper testing. If the patch testing is performed while the patient has active or flaring disease, he will often produce false positive test responses that have no meaning in terms of the patient's diagnosis and he runs a significant risk of causing a flare of the patient's pre-existing skin disease. It is most important that the doctor not apply patch tests to chemicals used in industry or brought in by the patient unless he is guided by proper testing dilution for each chemical. Failing to follow this rule can result in cutaneous burns at the test site. This irritant chemical response is of no diagnostic help and can at times cause the induction of allergy through testing.

The A1 test tapes are available from Imeco Astra Agency Company in Stockholm and the tests are applied in vertical rows on the upper back as shown in Figure 4. The tests are affixed to the skin with Dermicel Tape produced by Johnson & Johnson. This tape is used because it rarely causes allergic reactions on the patient's skin. The upper back is the desired site for testing as other sites may be either less or more reactive and the testing method must be standardized.[16] All tests are left in place for 48 hours and if only one reading is possible, we have the patient remove the tests at the end of 48 hours and return to our office at 72 hours for reading. It is a common experience to see a negative response when the tests are removed at 48 hours only to have a true allergic response visible at 72 hours.

Patient Management

When the patient comes into the doctor's office with contact dermatitis if it is limited to a part such as the hands, he is taught contact isolation or withdrawal from all chemical exposure in his environment that could possibly aggravate his disease. If the dermatitis is severe and widespread, covering 50% or more of the body, we prefer to hospitalize the patient and there carry on appropriate contact isolation. This means that the nurses allow no chemical exposure in the patient's hospital room other than the hospital linen, toothbrush, toothpaste, reading material, TV set, comb and eating utensils. All other chemical exposure such as toiletry articles, items a woman carries in her purse, proprietary salves, etc. are excluded from the hospital room. If our diagnosis is correct and we do not apply medications that contain an agent to which the patient is already allergic, by definition the patient must exhibit a rapid recovery.

Topical steroid creams are the treatment of choice in the subacute and chronic phases of the disease. When there is weeping, edema, vesiculation or a severe acute inflammatory response, a shake liniment is initially used three times a day after a room temperature plain water compress. I do not advocate the usage of medicated compresses as these only add to our chemical exposure; something we are trying to avoid. Calamine liniment is perfectly adequate in therapy during the first three or four days after compresses to bring down the weeping, swelling and acute inflammation of the skin. Once the edema, swelling, crusting and vesiculation has disappeared, we switch to the least expensive, effective, topical steroid cream and today triamcinolone appears to fulfill that need. If the problem is subacute with a fair amount of erythema, triamcinolone 0.1% cream is used. If the problem shows a greater degree of chronicity or shows a dull erythema with scaling and some dryness of the skin, we may use the following:

Rx. Triamcinolone 0.1% Cream 60.0
White petrolatum, qs ad 120.0

We can use any multiple of this prescription depending upon body surface area to be treated. Rarely does contact dermatitis present as an extremely chronic, lichenified, dry dermatitis. On this rare occasion, triamcinolone 0.1% ointment would be utilized.

We avoid the use of medications containing neomycin, ethylenediamine, ammoniated mercury, any and all of the 'caine' drugs, topical sulfonamides, thimerosal containing preparations or in other words medications which, as we have already seen, carry with them a prohibitively high sensitization index or contain chemical ingredients which can be found elsewhere in one's environment.

It has been my experience with the above approach that it is rarely necessary to treat the average patient with contact dermatitis with systemic corticosteroids. The only form of contact dermatitis that requires systemic corticosteroids with any frequency, in our experience, is poison ivy dermatitis. In poison ivy dermatitis the average dermatologist is rather quick to use a ten day to two week decreasing dosage of systemic corticosteroid such as Prednisone tablets. The reason for this is that the allergen in poison ivy, poison oak and poison sumac is such an intense allergen that it produces a spreading disease long after the poison ivy exposure is terminated. The disease response can be so severe with blisters and swelling that time loss from work, school and recreation becomes prohibitive. There is little risk in a ten day to two week decreasing dose of Prednisone tablets in this disease. The chronic use of systemic corticosteroids with any other form of contact dermatitis is seldom required.

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Bacterial Infections of the Skin

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A selected group of primary and secondary infections of the skin is presented. Their distinctive clinical features and appropriate management are stressed.

BACTERIAL INFECTIONS of the skin are a common affliction. Their prompt recognition together with appropriate therapy is imperative if significant complications are to be averted. Familiarity with their typical morphology often permits treatment on sight, whereas unusual or atypical eruptions demand laboratory assistance for proper diagnosis.

Classification of Bacterial Infections

It is necessary to distinguish primary and secondary infections. Those arising de novo on normal skin, incited by a single organism, and which have a characteristic morphology and course, are termed primary. They are most frequently caused by coagulase-positive staphylococci or beta hemolytic streptococci. Secondary infections arise as a complication of a pre-existing skin disease. A mixture of organisms may be found on culture and it may be difficult to assess which plays the major role. The course which follows may be uncharacteristic and prolonged. A classification of those entities under consideration is presented in Table 1.

TABLE 1

Selected Cutaneous Bacterial Infections

- I. Primary Infections
    - A. Pyodermas
        - 1. Impetigo
        - 2. Ecthyma
        - 3. Folliculitis
            - a. Superficial
                - (1) Impetigo of Bockhart
                - (2) Gram-negative folliculitis
            - b. Deep
                - (1) Sycosis barbae
                - (2) Furuncles and carbuncles
        - 4. Erysipelas and cellulitis
    - B. Erysipeloid
    - C. Erythrasma
    - D. Swimming pool granuloma
- II. Secondary Infections
    - A. Infectious eczematoid dermatitis
    - B. Bacterial intertrigo
    - C. Pyoderma gangrenosum

Ecology of the Skin

The dominant organisms of normal skin are aerobic staphylococci and diphtheroids; streptococci are rarely found.[1] Staphylococcus aureus is encountered occasionally, but it is never a plentiful organism. In an exudative dermatitis, however, Staphylococcus aureus may be recovered in abundance. A gram stain of such a lesion is helpful, for finding appreciable numbers of bacteria within polymorphonuclear leukocytes is indicative of true infection, rather than mere colonization.[2] The normal cutaneous flora consists of resident and transient organisms. Resident organisms are regularly present and are capable of multiplication and survival (Table 2).

TABLE 2

Resident Bacterial Flora[1,2]

- I. Aerobic Flora
    - A. Staphylococci
        - 1. Staphylococcus albus
        - 2. Staphylococcus epidermidis
        - 3. Micrococcus candidus
        - 4. Micrococcus flavus
    - B. Corynebacteria
        - 1. Lipophilic diphtheroids
        - 2. Non-lipophilic diphtheroids
    - C. Gram Negative Organisms
        - 1. Mima polymorpha
        - 2. Herellea vaginicola
        - 3. Enterobacter (Aerobacter) spp.
- II. Anaerobic Flora
    - A. Corynebacterium acnes
    - B. Micrococcus saccharolyticus

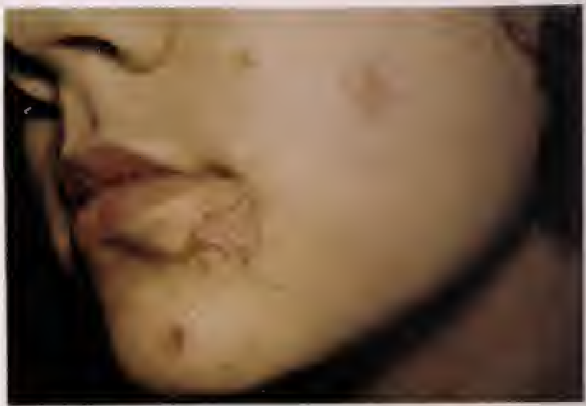

Fig. 1—Impetigo. Intact bulla on the cheek and varnish-like crusts on the chin.

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The transient flora consists of a multiplicity of organisms which are deposited on the skin from the environment. They do not proliferate and are easily removed by scrubbing.

General Therapeutic Measures

Recovery of the skin from bacterial infections is facilitated by restoring its structural integrity. Moisture favors colonization with bacteria, whereas bacteria die if they become desiccated. Reinstating the normal dryness of the skin is of utmost importance.

Though it may seem paradoxical, cleansing and drying are best accomplished by the application of wet dressings.[3] An open wet dressing applied for thirty minutes four times a day is particularly helpful.

Certain therapeutic principles are applicable to the treatment of all bacterial infections of the skin, and particularly the pyodermas. These principles are enumerated in Table 3.

TABLE 3

General Principles of Antibacterial Therapy

1. **Thorough cleansing of the skin**
2. **Remove crusts when present**
3. **Trim and clean nails**
4. **Prevent scratching**
5. **Proper antimicrobial agent for local use**
6. **Systemic antibiotic therapy when indicated**
7. **Infectivity precautions**
    a. **Separate towel and wash cloth for patient**
    b. **Change and clean clothing and bedding frequently**

Primary Bacterial Infections of the Skin

Impetigo

This very common superficial infection occurs most frequently on the exposed parts of the body. The eruption begins as erythematous macules soon becoming vesicles or bullae.

Impetigo contagiosa is characterized by thin-walled vesicles which rupture quickly and form adherent, honey-colored crusts. Satellite lesions, peripheral extension, and central involution lead to circinate and gyrate configuration.

Bullous impetigo (BI) is a variation having a predilection for infants and young children. The bullae last for several days before they collapse to produce a varnish-like crust (Figure 1). Pemphigus neonatorum (an obsolete term) refers to an extensive form of bullous impetigo occurring neonatally, often accompanied by a high fever. Bullous lesions are of staphylococcal origin in contrast to impetigo contagiosa which is due to beta hemolytic streptococci with or without secondary staphylococcal growth.[4-6]

An acute systemic reaction consisting of the formation of flaccid bullae and a painful exfoliative erythroderma is known as Ritter's disease or dermatitis exfoliativa neonatorum. This is either a variant of bullous impetigo[7] or a form of toxic epidermal necrolysis (TEN) or the scalded skin syndrome.[8-10] It differs from BI of the newborn by the tender "scalded" appearing symmetrical eruption in which the skin is shed in sheets on minimal trauma.

The causative organism in both BI and TEN is most frequently Staphylococcus aureus of phage group II, type 71.[8] The organisms isolated in TEN have been shown to produce a diffusable toxic factor termed "epidermolytic toxin.[11] Factors peculiar to host resistance rather than the causative organism determine the type of response. The staphylococcal scalded skin syndrome is usually considered a pediatric disease. Whereas drug induced TEN occurs in adults, there are only two well documented adult cases of staphylococcal TEN. In both instances the patients suffered from chronic renal disease.[12,13]

The use of systemic antibiotics in the management of impetigo is controversial.[14] Some would reserve it for the patient with extensive disease[3,15] whereas others believe it is the treatment of choice in all cases.[16] Prevention of acute glomerulonephritis due to nephritogenic strains of streptococci is of paramount concern. The incidence among patients with impetigo varies from two to five percent.[16,17] This occurs most frequently in children under six years of age. Little is known about the incidence of post impetigo nephritis in adults; however, in contrast to children in whom the prognosis is usually excellent,[18] in adults there is a poorer prognosis. No relationship has been found between the severity of the skin infection and the development of chronic renal disease.

Although lesion morphology is helpful, the etiologic agent cannot always be predicted on the basis of clinical appearance.[4] In children, regardless of the extent of the disease, systemic antibiotic therapy is advocated. Benzanthine penicillin G intramuscularly is effective even in the presence of resistant staphylococci.[4,6,19] Erythromycin is a good alternative in those allergic to penicillin. Good local care in accordance with

Table 3 is essential. An infant with BI should be isolated. Ritter's disease should be treated with a penicillinase resistant drug and fluid and electrolyte balance maintained.

Ecthyma

A deeper type of impetigo, usually caused by beta hemolytic streptococci, is known as ecthyma. It occurs most frequently on the legs and is characterized by vesiculopustules that produce a shallow ulcer by eroding through the epidermis. Large crusts develop which firmly adhere to the underlying erosion (Figure 2). Unlike impetigo, it does not spread peripherally. Variable scar formations occur as a result of extension into the dermis. Minor trauma, poor hygiene, and neglect are contributory factors.

The treatment is the same as for impetigo. Systemic antibiotics are usually advisable.

Folliculitis

Variable forms of folliculitis occur with the bacterial infection being either superficial or deep. Although coagulase-positive staphylococci are usually responsible, other organisms are occasionally accountable for this pyoderma.

Impetigo of Bockhart. The scalp and extremities are the sites most favored in this superficial pustular folliculitis characterized by tense, painful, dome-shaped pustules of the follicular ostia. It may be secondary to the application of topical therapy used in the treatment of other skin conditions. Crude coal tar or steroid creams under plastic occlusion are typical examples.

Gram-negative Folliculitis. Two varieties of this relatively uncommon complication of acne treatment are recognized:[20] Type I is characterized by superficial pustules about the nose, spreading out onto the cheeks. Type II consists of deep nodular and cystic lesions. The Enterobacter-Klebsiella species have been associated with Type I while Proteus has been found in the deeper lesions.[21]

Treatment is dependent upon antibiotic sensitivities, with ampicillin usually being the drug of choice.[20] As the nasal mucosa is believed to be the reservoir for the attacks of folliculitis, the topical application of antibiotic creams such as gentamicin to the anterior nose is salutary.

Sycosis Barbae. Frequently termed "barber's itch," this is a deep folliculitis of the bearded area. Pruritic follicular papules and pustules spread rather rapidly by shaving (Figure 3). With neglect, impetiginization and crust formation occurs. Differentiation from tinea barbae may be difficult. Potassium hydroxide examination of the involved hair, bacterial and dermatophyte cultures are necessary for evaluation.

Furuncles and Carbuncles

A furuncle is a more severe and extensive perifollicular staphylococcal abscess. Hairy and exposed skin subject to friction and maceration are the typical sites of involvement. Furuncles may originate from a preceding folliculitis or de novo as a deep nodule. Fluctuance may occur within four days as central necrosis and suppuration occur. This culminates in a yellowish apex with rupture ensuing and the expulsion of necrotic tissue. Furuncles may resolve without rupturing.

A carbuncle is a more extensive inflammation of several adjacent pilosebaceous units which drains through multiple openings onto the surface. With deeper involvement, a brawny appearance is noted. Large ulcerations with marked scarring may arise as a result of the extensive suppuration.

Hot packs followed by incision and drainage as the lesions reach maturity, facilitates the treatment of furuncles and carbuncles. Internal antibiotics are occasionally needed in recurrent and recalcitrant cases of superficial folliculitis, and essential in sycosis barbae, carbuncles, and severe cases of furunculosis. Recurrent furunculosis has been managed successfully by artificial colonization of the nasal mucosa with a staphylococcal strain of low virulence (strain 502 A) following the administration of a semisynthetic penicillin.[22] This strain of staphylococci interferes with the subsequent acquisition of more virulent strains. Protection against invasive Staphylococcus aureus through the use of vaccines and toxoids has been unsatisfactory.[23]

Erysipelas and Cellulitis

An acute inflammation of the skin and subcutaneous tissue characterizes these states. In erysipelas, the inflammation is superficial and a hot, red, edematous plaque with a raised indurated border results. Vesicles or bullae are occasionally noted. Constitutional symptoms and local lymphadenopathy occur. The organism is beta hemolytic streptococcus. The fact and scalp are sites of predilection. Recurrent attacks in the same area lead to persistent lymphedema. In cellulitis, which involves a diffuse spreading infection of deeper tissues, less well demarcated lesions with a more diffuse border arise. Streptococcus pyogenes is the usual cause. Rest, local wet dressings (cool for erysipelas and warm for cellulitis), and Penicillin G systemically for one week usually give a prompt and satisfactory response in these conditions.

Hemophilus influenzae cellulitis is an uncommon but distinctive form (Figure 4). The typical patient is between six and 36 months of age.[24] After a one to two day prodrome of nonspecific cough and fever, there is an explosive onset of a red, bruise-like circumscribed swelling of the face and less commonly of the extremities.[25] A bacteremia frequently accompanies this cellulitis and it may lead to metastatic meningitis, osteomyelitis, or pyarthrosis.[26]

It has been suggested that there is a direct spread of the H. influenzae from the oral cavity

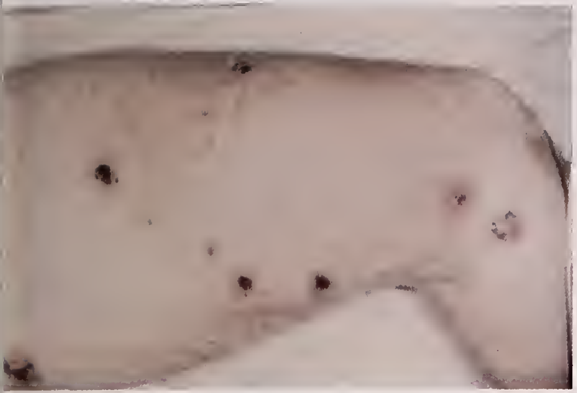
Fig. 2—Ecthyma. Multiple crusted lesions on the legs.

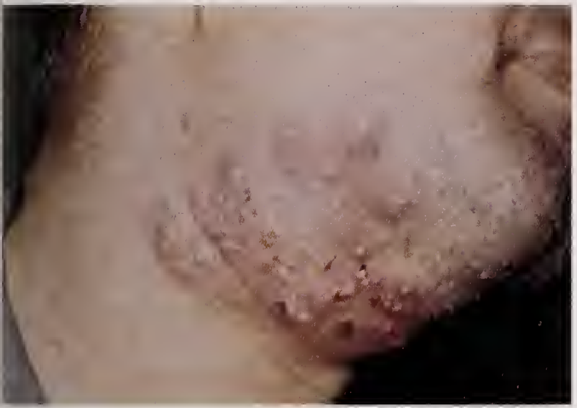
Fig. 3—Sycosis barbae. Multiple pinhead size pustules and a boggy infiltration of the skin.

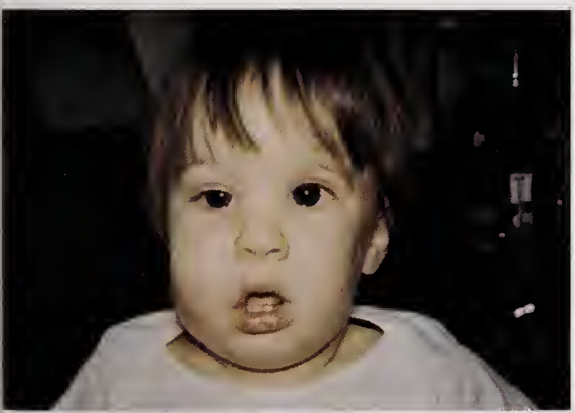
Fig. 4—Hemophilus influenzae cellulitis on the face of an infant.

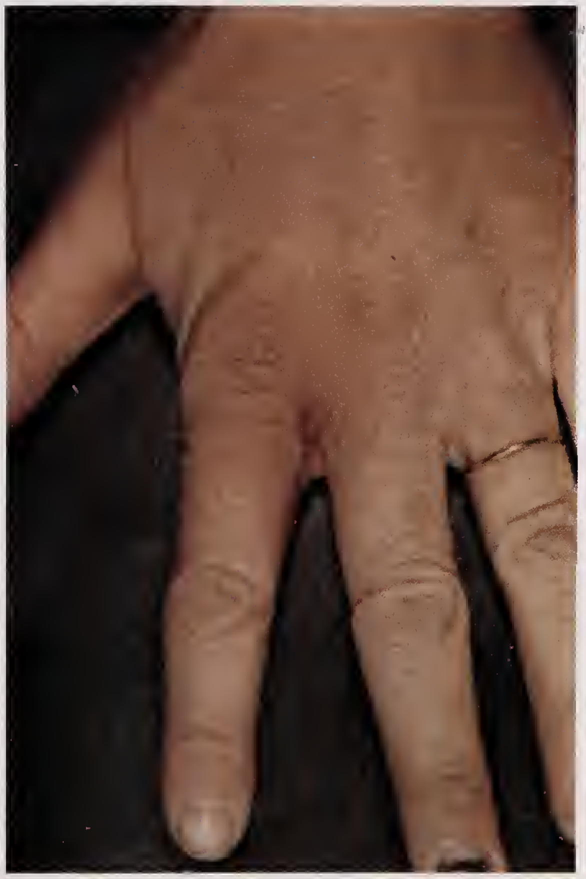
Fig. 5—Erysipeloid. A nonsuppurative cellulitis on the back of the hand.

to the cheek. The diagnosis may be confirmed by isolation of the organism from the blood and throat. Percutaneous aspiration from the border of the cellulitis may also be helpful. The prognosis is favorable when intravenous ampicillin, 150 mg. per Kg per day in divided doses is administered early.

Erysipeloid

This purplish, nonsuppurative cellulitis presents as a painful swelling usually on a finger, the back of the hand or wrist (Figure 5). It is seen most frequently in fishermen and meat handlers, and is caused by a gram-positive rod, Erysipelothrix rhusiopathiae. Fever and constitutional symptoms are usually mild or absent except when a more generalized eruption occurs. Diagnosis is made by culture of tissue specimens. Systemic penicillin is an effective remedy.

Erythrasma

Corynebacterium minutissium, a diphtheroid and a normal member of the skin flora, is the cause of this superficial bacterial infection. Brown, dry, slightly scaling and sharply demarcated patches affecting intertrigenous sites are characteristic. These patches show a coral red fluorescence on Wood's light examination.

The most effective treatment is erythromycin, 1 gram daily for two weeks.[17] Antibacterial soaps and topical tolnaftate (Tinactin) solution are useful adjuncts.

Swimming Pool Granuloma

Mycobacterium marinum, one of the atypical, mycobacteria, is responsible for this indolent granuloma which occurs at points of trauma. Beginning as erythematous papules, the lesions slowly enlarge to form red nodules. Usually no necrosis or ulceration occurs, however, the lesions may become very verrucous in appearance.

Generally a localized infection of the elbows, knees or nose occurs following an abrasion of the skin while swimming in contaminated water. Multiple nodular sporotrichosis-like infections have also been reported.[27,28] Tropical fish aquariums are another source of infection.[28]

The organism grows best at 32°C and poorly at 37°C.[26,29] There is no specific therapy. Small lesions should be excised completely. Xrays, electrosurgery, cryocautery, and local application of heat may be helpful.

Secondary Bacterial Infections

Infectious Eczematoid Dermatitis

This term is applied to the development of an eruption about a primary source of an infectious exudate such as a draining ear, abscess, or ulcer Vesiculopustular plaques spread peripherally from the local source and become secondarily crusted. Spreading to distant sites can occur presumably due to autosensitization. Coagulase positive staphylococci are most frequently isolated.

Treatment of the primary source of infection is essential. Cultures and antibiotic sensitivities determine what antibiotic to use. The same principles of management used in primary pyodermas are applicable here. A combination antibiotic-steroid cream may be applied.

Bacterial Intertrigo

The macerating effects of heat, moisture, and friction are productive of this superficial inflammatory eruption which occurs in intertrigenous sites. Obesity, diabetes mellitus, urinary and fecal incontinence are predisposing factors. Bacterial infection readily occurs as exudation and dissolution of the stratum corneum develop. The favorite sites are the axillae, groin, intragluteal cleft, inframammary region, and between the toes. Some cases designated as "athlete's foot" are, in reality, another instance of intertrigo.

The elimination of maceration is the *sine qua non of treatment*. Separation of the opposing surfaces by gauze dressings and the application of a talc dusting powder is beneficial. More severe cases require wet dressings. Appropriate antibiotics should be applied locally.

Pyoderma Gangrenosum

Bacteria play no primary role in pyoderma gangrenosum (PG). Although many organisms may be found secondarily, there is no proof of a primary bacterial cause.[7] Bacteriologic studies have not revealed any specific organisms and, in fact, early lesions may be sterile on culture.[30]

Initially an erythematous papulopustule appears which rapidly becomes necrotic within two days. As central ulceration occurs, the lesion extends peripherally to become a plaque several centimeters in diameter. There is a violaceous discoloration of the liquefactive margin. A halo of erythema around the ulcer foretells that additional tissue is becoming involved.

The rapidity of development, the kaleidoscopic array of colors, and the severe local pain which accompanies these rapidly developing ulcers, are the hallmarks of PG.

The management of these phagedenic ulcerations must take into consideration any associated disease. Perry noted 50% of 62 patients studied at the Mayo Clinic had chronic ulcerative colitis (CUC).[31] Nine of the remaining 31 patients also had gastrointestinal disease. In addition to CUC, diverticulosis, regional ileitis, and peptic ulcers have been other gastrointestinal manifestations. Other recorded associations have been systemic pyogenic infections, polyarthritis,[32] lesions resembling dermatitis herpetiformis,[33] leukemia,[34] paraproteinemia, and myeloma.[35] Occasionally, PG may arise independently of any systemic disease.

Sulfapyridine 4 to 8 grams daily in divided doses has been successfully employed in the management of PG.[31] Systemic corticosteroids are invaluable in the more severe cases. Cleansing tub baths and potassium permanganate wet dressings are useful locally applied measures.

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Gratitude

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The Editors
MINNESOTA MEDICINE

Warts

Biology and Current Therapy

FRANKLIN PASS, M.D.*

Warts are common, benign growths caused by human papilloma virus. Warts generally disappear without treatment but may become large and longstanding. Physicians use simple destructive methods to treat warts, but frequently patients try a variety of folk medicines. Current therapy is often not successful, but newer methods are being investigated. Research is directed toward understanding the mechanisms of spontaneous regression and the relationships between the virus and the epithelial cell. Specific immunotherapy and newer anti-viral drugs offer promise.

HUMAN WARTS (verrucae) are benign tumors of epidermal origin caused by human papilloma virus (HPV). Although warts usually disappear spontaneously, they frequently proliferate in an uncontrolled fashion causing discomfort to the patients and headaches for physicians. There is no consistently effective method to prevent or treat warts, but understanding the biology of warts may help prevent needless or harmful therapy. This brief review ranges from folklore to molecular biology, but the objective is to assure the practitioner that help is on the way. Interested readers should refer to the comprehensive and still current review by Rowson and Mahy.[1]

Clinical Problem

Warts generally occur at favored locations on the skin or adjacent mucous membranes, but any site may be involved. Trauma or infectious spread may account for the common warts on fingers or periungual skin (Figure 1). Small, flat warts spread over the dorsum of the hands and the face by autoinoculation from scratching. Filiform warts in the beard area of males are similarily spread by shaving. Plantar warts are often localized to pressure points over the heads of the metatarsals or the heel, but may extend over the dorsum of the foot (Figure 2).

The clinical appearance of warts varies from one location to another, but these differences are only in the degree of keratinization or amount of epithelial proliferation. All warts are well circumscribed areas of epithelial thickening (Figure 3). The mass is not uniform but consists of irregular downward proliferations of epidermal ridges or pegs (rete). The germinative epidermal cells (keratinocytes) appear normal. Foci of vacuolated keratinocytes are seen in the higher stratum granulosum, and the stratum corneum is greatly thickened. These microscopic changes correspond to the sites where virus particles (virions) are observed by electron microscopy.[2] Viral DNA synthesis appears to be limited to the vacuolated cells of the stratum granulosum.[3]

Genital warts present a special clinical problem because of rapid and exuberant growth and resistance to therapy. Epidemiologic studies indicate that genital warts are spread in a venereal pattern with an unusually high prevelance amongst male homosexuals.[4] Serologic studies from one laboratory suggest that genital wart virus may differ from common wart virus in antigenic structure,[5] but others[6] have not supported this contention. To date, virions have not been purified from genital warts, and it may be best to consider all warts due to a single virus, HPV.

Laryngeal papillomas occur at any age, but present an unusual and serious problem in young children. These children may contract the papillomas during delivery, and then require multiple surgical procedures over a period of years. Early in the disease, airway obstruction can be prevented by tracheotomy, but spread of the papillomas to the bronchi may result in death by suffocation. Most investigators believe that laryngeal papillomas are caused by HPV, and a recent electron microscopic study visualized HPV-like virions in papilloma tissues.[7,8] As is the case with genital warts, our knowledge of laryngeal papillomas can only be increased by further virologic studies.

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Current Therapy

Current therapy of warts is based largely on destructive measures listed in the Table. The rationale is sound, i.e., the pathology is limited to the epidermis, and these procedures either directly destroy or cause the subepidermal separation of the tumor mass. However, the effectiveness of any single modality is limited by the size and thickness of the wart. These restrictions often result in many office visits and expenses which outweigh the banal nature of the problem. The enthusiasm of the therapist must be tempered by the potential for scar formation. The majority of warts dis-

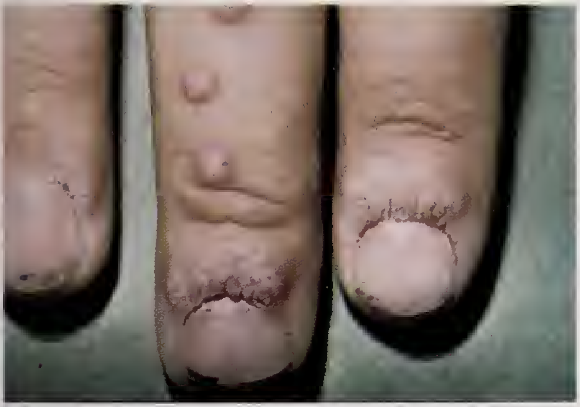

Fig. 1—Common warts and periungual warts.

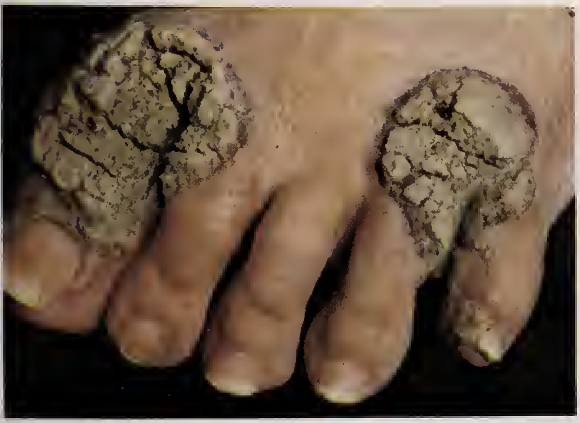

Fig. 2—Unusually large warts extending over the dorsum of several toes.

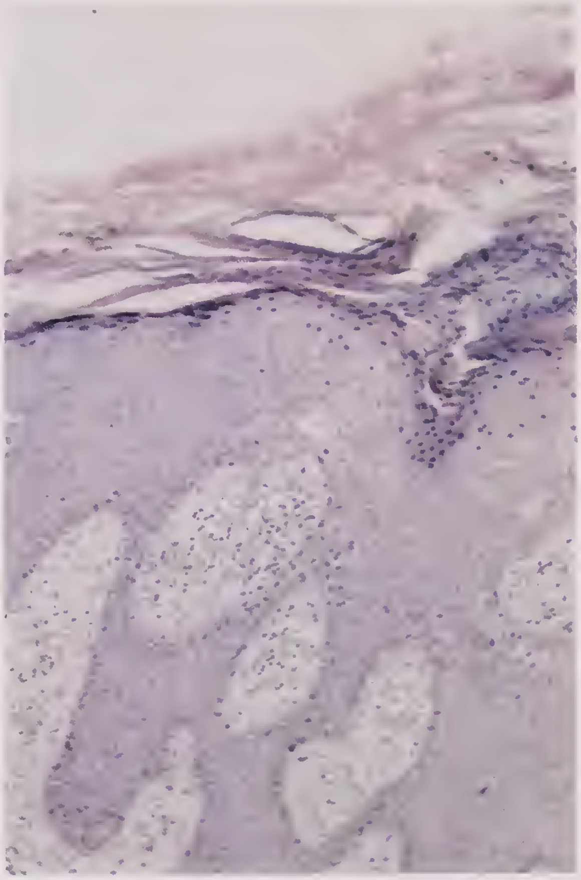

Fig. 3—Hematoxylin and eosin stained section from wart pictured in Fig. 2. A focal area of enlarged, pale cells begins at the stratum granulosum and extends upward in the thickened stratum corneum. Original magnification x 200.

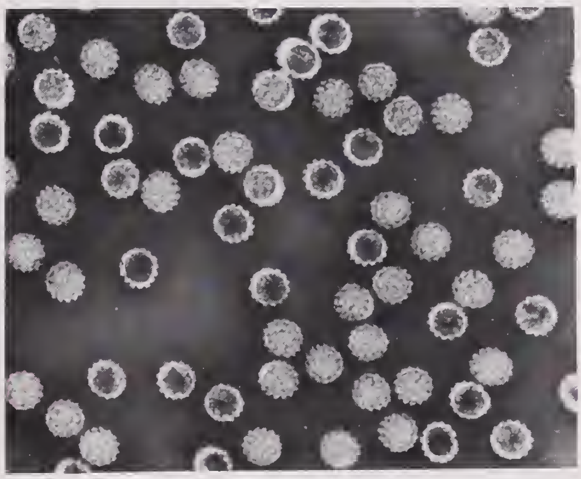

Fig. 4—Human papilloma virus (HPV) virions viewed by the electron microscope after negative staining with phosphotungstic acid. Doughnut shaped virions do not contain DNA and are referred to as "empties". Virions are 53 nm in diameter.

appear spontaneously after an average period of two and a half years,[9] and spontaneous regression leaves no scar. For patients with multiple warts, most dermatologists advocate gentle procedures like the repeated application by the patient of an acid preparation (the author uses 10% salicylic acid in flexible collodion) while biding time for spontaneous recovery.

TABLE

Current therapy for warts. Destructive measures are common office procedures. Immunotherapy and chemotherapy are newer, experimental procedures.

Destructive Therapy
Electrodesiccation
Curettage
Liquid Nitrogen
Acids
Cantharidin
Podophyllin

Immunotherapy
Dinitrochlordbenzene (DNCB)
Small Pox Vaccine
Autologous Wart Vaccines

Chemotherapy
5-Fluorouracil
Bleomycin

Local irradiation of warts, which are refractory to destructive procedures, is used by some radiotherapists in Minnesota, but the advent of newer experimental procedures discussed below has already reduced the need for x-ray therapy. Recurrence may follow x-ray therapy as is seen with other modalities.

Many patients depend upon folk remedies for treating warts. The most famous of these was offered by Tom Sawyer: ". . . backing up to the stump, placing the hand with the offending wart into the water, and reciting: 'Barleycorn, barleycorn, Injun-meal shorts; skunk-water, skunk-water swaller these warts!' " Minnesotans seem to depend more on milkweed sap than skunk-water, but many remedies are based upon some suggestion to the victim that the warts will soon disappear. Dermatologists occasionally paint a child's warts with fluorescein and then shine an ultraviolet Wood's lamp on the warts in a dark room. The author knows a pediatrician who embellishes this routine by having his nurse stand behind a screen and beat on a metal dishpan. These methods may succeed by hypnotic suggestion, and recently investigators reaffirmed the positive effect of hypnotherapy.[10] Equally, or more plausibly, success may depend upon spontaneous regression.

Basic Virology

HPV is one of the several papilloma viruses infecting mammalian species. The papilloma viruses are a subgroup of the papova viruses, and papova is an acronym standing for papilloma (pa), polyoma (po) and vacuolating (va). These are all oncogenic DNA viruses of similar size and structure. HPV was one of the first viruses to be passed by inoculation[11] and visualized by the electron microscope.[12]

In our laboratory parings from plantar warts are saved as a source for virus. Virions are purified by grinding the tissues to a paste with silicon carbide in phosphate buffer.[13] The tissue and silicon carbide are removed by low speed centrifugation and purified virions are isolated by equilibrium density centrifugation in cesium chloride. Virions may be viewed in the electron microscope after staining with 1% phosphotungstic acid (Figure 4). Virions contain a central core of double stranded, superhelical DNA, but only the protein capsid is visualized. The capsid is composed of 72 subunits called capsomeres.[14] When the proteins of the virions are dissociated in heated detergent, they may be separated and studied by polyacrylamide gel electrophoresis. Approximately 85% of the protein is a single polypeptide with an estimated molecular mass of 53,000 daltons.[13] The viral DNA may also be isolated from dissociated virions. Sedimentation gradients run in alkaline sucrose solution define two types of DNA, which represent double strands and denatured single strands.[15]

Immunologic Studies

Spontaneous disappearance of warts may be an immunological phenomenon. Warts are more common in children, and frequently after treatment of one wart other untreated warts disappear. Clinically, regression may be accompanied by inflammation or hemorrhagic infarction and histologic changes suggesting an immunological event. The difference between infarction and inflammation has been noted histologically; an Arthus-like reaction[16] and a cellular immune reaction[17] have both been reported. Renal transplantation patients treated with immunosuppressive medications develop multiple, non-regressive warts,[18] which is the most suggestive clinical evidence linking immunity and regression. Similarily, occasional patients with multiple warts manifest defects in humoral or cellular immunity.[19]

Regression may be mediated by humoral or cellular immunity directed toward virion antigens or special tissue antigens present in warts. About 20% of patients with warts have antibodies to the virion.[20] Some authors have suggested that antibodies correlate with regression,[16,21] but others believe this is not the case.[22,23] In our studies, antibodies were the IgG type directed toward the capsid polypeptides,[13] and the presence of antibodies correlated with the number and duration of warts, not disappearance. Tumors in animals caused by viruses related to HPV contain new antigens, which are glycoproteins coded for by the viral genome but not a part of the virion structure.[24] These antigens are related to transplantation antigens and stimulate a host immune response to control the tumor. The search for wart-specific antigens has not as yet succeeded, but cell surface changes in warts have been observed.[25] Cell-mediated immune responses to virion or tissue antigens have not been studied.

Investigators have already manipulated the immune system to treat warts.[26,27] Patients were sensitized to the topical application of dinitrochlorobenzene (DNCB), a hydrocarbon haptene, and after sensitization, patients applied ointments containing DNCB to their warts. The ensuing cell-mediated immune reactions (eczema) often caused the treated warts to disappear, and occasionally, distant untreated warts disappeared, as well. This concept has also been explored using small pox vaccine,[28] but the potential complications of intralesional small pox vaccine therapy are much greater than DNCB.

Other avenues of immunotherapy have been or are currently being studied. One group of investigators administered autogenous vaccines from wart tissues,[29] but vaccines containing oncogenic viruses may be dangerous and must be studied only by experienced virologists. Another approach may be the use of transfer factor, an extract prepared from immune lymphocytes. Transfer factor has been useful in treating patients with severe mycotic infections,[30] and efforts to treat patients with warts are now in progress at several medical centers. The current problems with this approach can be attributed to our ignorance in selecting specific donor lymphocytes.

Studies of Molecular Virology

The final understanding of warts depends upon uncovering the fundamental relationship between HPV and the epithelial cell (keratinocyte). How does the infectious viral DNA enter the keratinocytes, and what subsequent events cause the keratinocytes to proliferate? Two types of infection have been observed in studies of related papova viruses: one type is called replicative or productive, because virus reproduces itself releasing more infectious virions to recruit adjacent cells; the other type is called transformation, whereby the viral genome is integrated into a germinative cell so that heritable changes in the growth of the cell are passed on to all the progeny.[31] Transformed cells resemble cancer cells, but replicative infections occur in otherwise normal cells.

It has not been possible to distinguish between replicative and transforming infections, because HPV has not been reproducibly propagated in a tissue culture system.[32] The study of keratinocytes from warts maintained in tissue culture may resolve this problem.[33] A radioactive labeled RNA transcribed from HPV viral DNA can be used as a probe to localize the viral DNA in wart tissues, and wart keratinocytes in tissue culture. This method has been used to study rabbit papillomas, and the Shope viral DNA was found only in keratinizing cells suggesting a replicative infection.[34] Studies of enzyme systems in human warts favored transformation rather than replication.[35] Investigators were able to distinguish two isoenzymes (A and B) of glucose-6-phosphate dehydrogenase (G6PD) in the normal skin of heterozygous females, but warts from these women contained only enzyme A or B. According to these data, a wart is a clone of cells arising from a single transformed keratinocyte.

If HPV causes only a replicative infection, newer anti-viral drugs may effectively block replication and cure warts. Fluorouracil has had limited therapeutic success in treating warts, and bleomycin is used commonly to treat warts in Japan.[36] Experiments are now in progress to test newer anti-virals related to known nucleoside analogs. Transformation presents much greater therapeutic problems, because anti-viral drugs would not be expected to affect transformed cells. In this situation an immunologic solution would hold more promise, or until that time, we can always dispense more skunk-water!

References on page 852.

Pediculosis Today

MILTON ORKIN, M.D.*

Infestations with pubic and head lice have recently resurged as substantial public health problems. The diagnosis, once considered, can be easily and quickly confirmed by identifying the parasite. Therapy is simple and effective. A high index of suspicion is necessary to prevent the progression of this epidemic.

IT IS PROJECTED that in 1974 there will have been about three million cases of pediculosis (lice) in the United States (50% more than in 1973); this approximates the estimated incidence of gonorrhea in the same years.[1] Lice are obligate parasites which infest humans in three forms: (1) Pubic or "crab" lice (Phthirus pubis), (2) Head lice (Pediculus humanus capitis), and (3) Body lice (Pediculus humanus corporis). The increment has been mainly in the pubic, and the head lice (involvement with body lice has increased slightly or remained the same). There has been a concomitant increase in infestations with scabies in most parts of the world.[2-4] The increase in pediculosis has occurred without regard to socio-economic barriers. Unexplained is the relative immunity of blacks to lice infestations.

Pediculosis Pubis

This form has become epidemic in the United

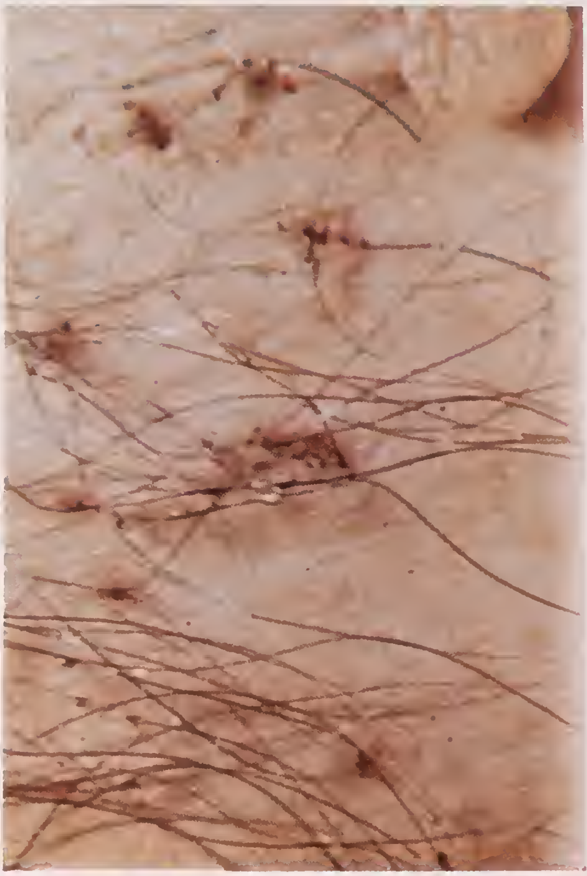

Fig. 1—Pediculosis pubis—Numerous nits (eggs) attached to pubic hair.

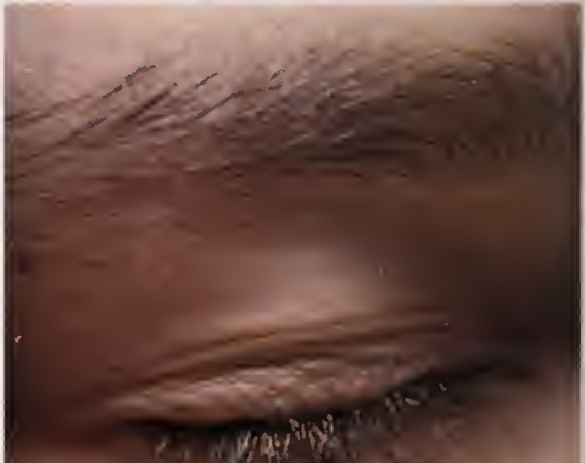

Fig. 2—Phthiriasis palpebrarum (infestation of eyelashes by pubic lice. Nits at base of cilia.

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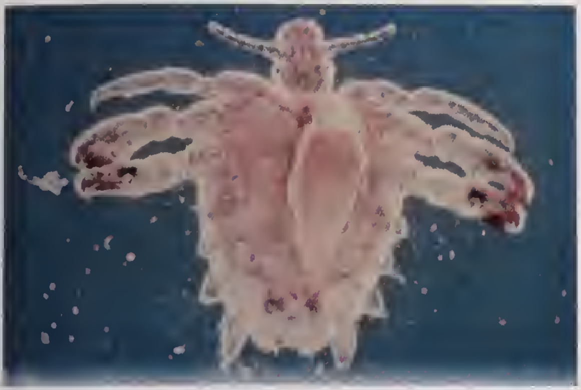

Fig. 3—Phthirus pubis—Broad crab-like body with powerful claws (second and third pairs of legs) which clasp hairs and are means of locomotion.

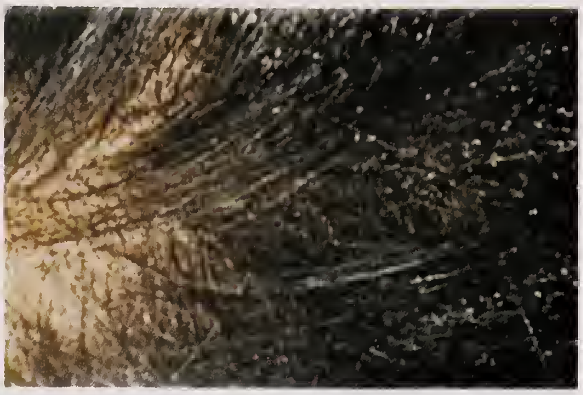

Fig. 4—Pediculosis capitis—Myriads of nits attached to hair at occipital scalp.

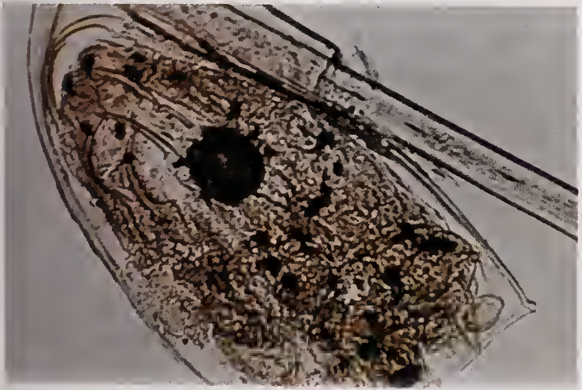

Fig. 5—Pediculosis capitis—Nit attached firmly to scalp hair.

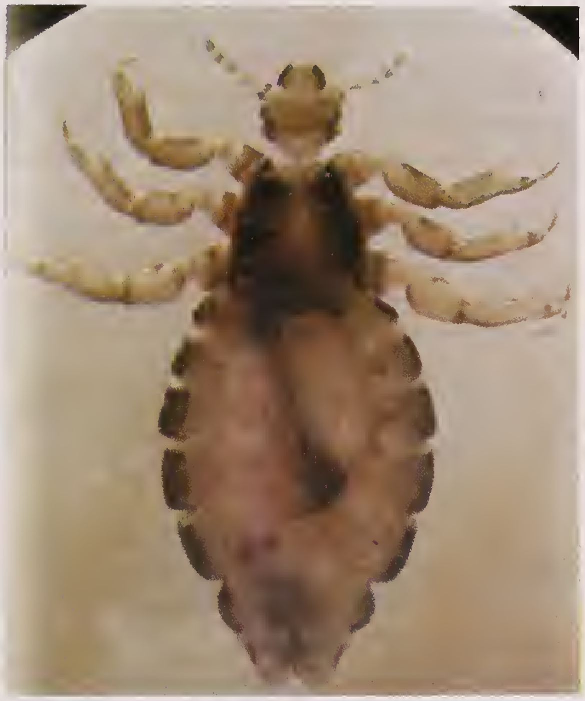

Fig. 6—Pediculosis corporis—Body louse (similar to head louse) easily differentiated from crab louse.

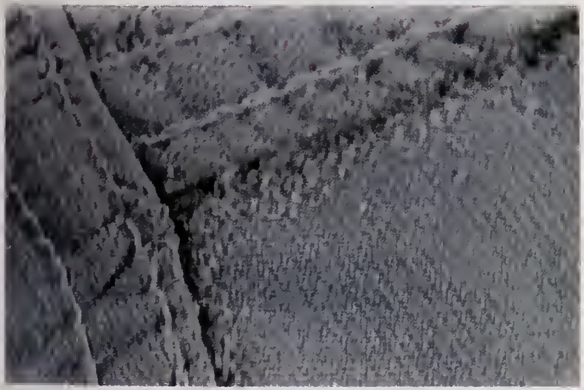

Fig. 7—Pediculosis corporis—Nits usually found on clothing seams rather than attached to hairs.

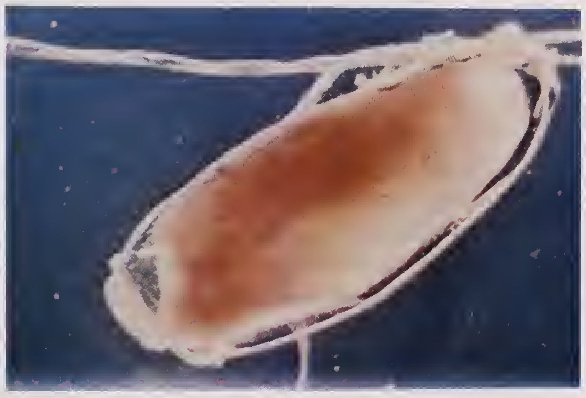

Fig. 8—Pediculosis corporis—Nit of body louse attached to clothing fiber.

States. The recent sexual revolution has played a vital role in this epidemic, particularly in young, unmarried individuals, since the condition is typically transmitted by sexual contact.[5] As in gonorrhea, the condition is more common in females, aged 15-19 years, and in males over the age of 20.[6]

As the name implies, the most common site affected is the pubic region (Figure 1). Although the organisms do not move much from the initial site of contact, involvement may occur, especially in hairy individuals, on the short hairs of the thighs and trunk, and on the beard and mustache. Involvement of the eyelashes (Figure 2) and periphery of the scalp occur mainly in children, with transmission likely from close contact with an infested mother. Pruritus, probably in large measure the result of allergic sensitization, is the common symptom; excoriations may lead to impetigo and pyoderma (which may mask the parasites) with lymphadenitis and febrile episodes.

Characteristic, but not always present, are the maculae caeruleae (sky-blue spots) which are unique, asymptomatic, bluish or slate-colored macules located on the trunk and thighs, fading within a short period. They are probably due to altered blood pigments of the infested human, or to an excretion product from the salivary gland of the louse.

Pediculosis pubis frequently co-exists with other venereal diseases, particularly gonorrhea and trichomonas and to a lesser degree scabies, nongonococcal urethritis, genital warts, candidiasis, and syphilis.[6] The diagnosis of Pediculosis pubis should initiate a search for these other conditions, beginning with a serologic test for syphilis.

Adult organisms are relatively few; they are easily distinguished from head and body lice (Figure 3). Although initially difficult to identify on the patient, the parasites become more discernible after a blood meal when they become rust-colored. The diagnosis is more frequently made by identification of the eggs (nits) which are attached by a cement substance to the pubic hair, initially at its junction with the skin. Since the ova grow out with the hair, the approximate duration of the infestation can be judged by the distance of the ova from the cutaneous surface. This is also true of Pediculosis capitis. The diagnosis is easily confirmed by plucking the hair, placing it on a clean slide with coverslip, and studying it under low power of the light microscope. The predilection of the "crabs" for pubic hairs is probably related to hair density, pubic hair being more widely spaced than hair elsewhere; the space matches the hindleg span of the pubic louse which moves by the four hindlegs clinging to two hairs.

Therapy

Therapy is almost the same as for scabies.[4] Gamma benzene hexachloride 1 percent (Kwell) is the most extensively used pediculocide and is my first choice. Benzyl benzoate is also used. These preparations are relatively pleasant, simple to use, and usually effective. The technique of usage is critical.

Gamma Benzene Hexachloride. All persons (affected or unaffected) living in the household should be treated; in addition, sexual contacts outside the household should be treated simultaneously. For convenience, therapy is usually begun in the evening, with all household members (afflicted persons last) taking a warm soap and water bath utilizing a soft brush, followed by drying with a towel. If there is any scalp involvement, Kwell shampoo may also be used. Kwell lotion is applied from the neck downward, with particular attention to hairy areas around the groin and perianal region, and allowed to dry. The liquid should be kept away from the eyes and mucous membranes, especially in children. Lotion is reapplied the morning and evening of the second day, and the morning of the third day (a total of four applications). The third evening a second bath, similar to the first, is taken but the lotion is not applied. All members then change underclothing, pajamas, linen, and so forth, and these articles are boiled, laundered, or washed by machine.

Therapy of eyelash involvement formerly consisted of applications of yellow oxide of mercury (still effective) but currently the use of anti-cholinesterase preparations is favored.[7] Eserine ophthalmic ointment (0.25%) applied thickly twice daily for 8 days is effective therapy. I believe that the patient should be seen simultaneously by an ophthalmologist because of possible eye symptoms and signs associated with the therapy. Therapy with eserine should be limited to those members of the family with definite ciliary infestation. The scalp should also be treated with Kwell shampoo, on two occasions at four-day intervals.

A problem is posed by the nits, with their impenetrable covering, gelatinous cement attached to hair, and incubation period of seven to eight days. Nits are, therefore, more persistent and resistant to therapy, and may have to be removed manually, usually by combing out with a fine toothed comb. Some prefer to retreat at eight to nine days if nits persist; retreatment is mandatory if new nits develop at the hair-skin junction.

Therapeutic failure is usually due to failure to follow instructions completely, neglecting to treat all affected members of the household or sexual contacts aside from the household, or reinfestation from a new outside source. Drug resistance, recently observed in scabies, has not been prominent in pediculosis. Occasionally pruritus persists even without flare of the cutaneous lesions. This may be due to irritation (usually from too frequent usage) of the pediculocide, irritation or sensitization to previous medications, or patient anxiety. Parasitophobia is not uncommon, with or without preceding pediculosis, and is difficult to deal with.

Pediculosis Capitis

This condition is being seen much more frequently, particularly (but not exclusively) in preschool children of both sexes. As soon as children are old enough to attend school the frequency decreases rapidly in males but continues in females. There have recently been a number of regional epidemics of head louse infestations in New York state, Indiana, Michigan, and British Columbia,[8] etc., in some instances necessitating temporary closing of schools. Since 1963, there has been an alarming resurgence in the United Kingdom, estimated at 1 million infestations in 1970 (Busvine-personal communication to Gratz[9]). Gratz[9] speculated that the recrudescence of head louse infestations in Europe might be explained by recently detected resistance of the head louse to some insecticides. The condition is much more common in cities than in rural areas.

The infestation is communicated by shared hats, combs and brushes, and promoted by long hair and elaborate hair styles, particularly those which discourage frequent washing and good hygiene.

Pediculosis capitis is typically confined to the scalp, particularly the occipital region, and to a lesser degree the post-auricular region. Pruritus is a cardinal symptom; excoriations frequently lead to impetigo and pyoderma with the hairs matted by the exudate. Regional lymphadenopathy and febrile episodes are not uncommon.

As with pubic lice, there are relatively few adult organisms, but there are myriads of oval nits cemented on the hairs (Figures 4 and 5). The nits, with their firm adherence (they are cemented) to the hairs, can be differentiated from seborrheic scales and hair casts, which can easily be moved along the hair shaft. Rapid examination of a large number of children (e.g., an entire school) is facilitated by Wood's light examination of the scalp which rapidly identifies the nits.

Therapy consists of Kwell shampoo to be used by the entire family and other close contacts (household, school, institution). The scalp should be thoroughly shampooed with two consecutive rinses lasting about three minutes each. The shampoo should be repeated four days later. Combing with a fine-tooth comb will remove any remaining nits. If nits persist at eight to nine days, and particularly if new nits develop at the hair-skin junction, retreatment should be instituted.

Pediculosis Corporis

This condition is rare in the Western World except in the very poor, vagabonds or those with low intelligence, with a predilection for unmarried men. The infestation is transmitted primarily by contaminated clothing or bedding.

Clinically the condition appears as numerous vertical excoriations, secondary to intense itching, especially on the trunk and neck. Secondary impetigo and pyoderma frequently supervene. Vagabond's disease is not merely Pediculosis corporis but also has facets of nutritional disturbances, post-inflammatory pigmentation, dirt, etc. The body louse is the only louse whose feces may transmit systemic diseases, viz., typhus, relapsing fever, and trench fever. Louse-born typhus and relapsing fever are still reported, mainly from Africa.[10]

There are very few or no adult organisms involved (Figure 6) but numerous nits are found on seams of clothing (particularly at the axillae, beltline and collar) where the organisms cling while feeding on the human host (Figures 7 and 8). The parasites may be entirely absent from the body even in a heavily infested person. The eggs cannot survive for longer than one month in stored garments.

Therapy mainly consists of proper hygiene, i.e., bathing plus change of underclothing and bedding is usually adequate for cure. These articles of clothing and bedding should be laundered or boiled. Kwell lotion can be used for occasional nits on the body hair in the same manner as in treatment for Pediculosis pubis. As in the other forms of lice infestation, all likely contacts (members of the household, contacts in institutions, etc.) should be examined and treated prophylactically. Rapid action must be taken to prevent spread through a community.

Acknowledgment

Figures 1, and 3 thru 8 were courtesy of Reed & Carnrick Labs, and Dr. A. Bernard Ackerman.

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What's New in Topical Therapy?

KENNETH P. MANICK, M.D.*

The failure to select appropriate topical therapy can result in secondary infection, sensitization, irritation, systemic absorption, and persistence and progression of the disorder, with possible dissemination or generalization. Rational and individualized topical therapy belongs in the therapeutic armamentarium of every practicing physician.

The judicious and rational utilization of topical or external therapy is frequently the most efficacious method for the treatment and alleviation of a variety of dermatological disorders, despite recent advances in systemic therapeutic management of a number of cutaneous conditions. The purpose of this paper is to present in simplified fashion a few principles of traditional topical therapy, with particular emphasis on the selection of a vehicle appropriate to the stage of an inflammatory cutaneous disorder, and to indicate some of the newer vehicles and medications employed in the topical management of these disorders. It does not represent an attempt to provide an exhaustive or comprehensive review of traditional or modern topical therapy, which would require a large text.

The treatment of dermatitis does involve a number of basic principles as incorporated into Table 1 below, which illustrates the selection of the vehicle into which active therapeutic medication can be added, or obtained in combination form, in pharamaceutical preparations.

While the vehicles are often relatively inert pharmacologically, they may contribute therapeutic activity related to their soothing, cleansing, lubricating or drying effects. In the Table, it can be seen that the vehicle should be selected on the basis of the stage of the cutaneous disease process, which may be of an acute, subacute or chronic character. Obviously, notable exceptions to this simplified approach exist, as for example in the reluctance of most informed therapists to employ a greasy ointment preparation for chronic dermatitis in moist, intertriginous or hairy areas, which

TABLE 1
Principles of Topical Skin Therapy
Treatment of Dermatitis

Stage of Disease	Clinical Manifestations	Selection of Traditional Vehicle (Active Therapeutic Medication to be Added)	Newer Vehicles
Acute	Erythematous Vesicular Weeping Edematous Tender Itching "Hot"	Open Wet Compresses (Drying)	Aerosols Solutions Lotion Formulations Gels More Lubricating Creams
Subacute	Less of the Above	Lotions, Creams (Less Drying)	
Chronic	Dry Scaling Thickened	Ointments (Lubricating)	Ointments (Lubricating)

Adjunctive Therapy: Baths, Powders, Linaments, Pastes

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may be cosmetically unacceptable and set the stage for secondary infection and irritation. Similarly, shake lotions in hairy or moist areas may "cake" and irritate, and more appropriate vehicles might be selected for these sites.

Among the many other factors to be considered in the treatment of dermatoses is the extent of the involvement, as represented by the percentage of cutaneous surface area included in the disease process, and the degree of inflammation, as manifested in the severity of the clinical expression and systemic signs. These two factors may place practical limitations on the type of preparation to be selected, relating in part to the cost of the preparation and to the degree of difficulty in application over large areas of the body. In addition, the potential for systemic absorption of the medication is relatively greater in severely inflammed skin involving a large surface area. The potential for sensitization to the ingredients of the medication or vehicle may also be increased by these factors. The age of the patient may also be important in this regard, as the infant, with his relatively greater proportion of surface area in relation to weight and poorly developed skin, may be a candidate for significantly enhanced percutaneous absorption. Further, the site of involvement may be a factor of importance, as illustrated by the hairy, moist or intertriginous areas cited above. It can be easily appreciated, therefore, that while Table 1 presents a number of basic principles which may be useful in approaching topical therapy, the treatment must be carefully designed to meet the specific needs of the individual patient. In general, it is best to select the medication-vehicle complex which offers the smallest concentration of the drug which will be effective along with the least sensitizing potential and cosmetic and cost acceptability to the patient. It is important to carefully outline for the patient detailed instructions related to proper use of the preparation, in order to meet these criteria. This is particularly true in the patient with a relatively chronic dermatological condition.

In acute dermatitis, the properly applied open wet compress offers cleansing, soothing, protective and cooling properties which alleviate a considerable portion of the discomfort associated with the clinical manifestations listed in Table 1. It is important that the wet compress be left open to the air, as the evaporation of the water, with its attendent local cutaneous vasoconstriction, is a major mechanism in producing the therapeutic effect. Tap water is the usual vehicle employed in the wet dressing. While a number of medications are utilized, perhaps the most common is Burow's solution in a 1:32 dilution (one ounce of Burow's solution to one quart of tap water) in a basin or pan maintained at room temperature. Several layers of soft cloth, such as bed linens, handkerchiefs, diapers, towels, Kerlix gauge or prepared derm-packs are dipped into the mixed solution, applied smoothly and snugly to the affected skin surface, and allowed to evaporate. Plastic wrappings or other obstacles to free evaporation are carefully avoided. When the compress begins to dry, which may vary from five minutes to several hours depending on the type of cloth employed, the compress is removed, resoaked in the solution and reapplied as before. While the hospital patient might have continuous (reapplication every two hours) wet dressings for some 48 hours, the outpatient can be instructed to utilize this mode of therapy as often as possible for at least 30 to 60 minutes three or four times daily. Lotions or creams may be applied between periods of wet compressing, as outlined below. The basin solution should be discarded and remixed once or twice daily, as it becomes concentrated and debris-laden.

As the acute dermatitis becomes subacute in terms of elapsed time and reduced severity of clinical and systemic manifestations, lotions or creams are employed, as continued use of wet compresses has a macerating and drying effect. Lotions are suspensions of powder (Kaolin, Talc, etc.) in a liquid vehicle (usually water), in which soothing and cooling effects ensue with evaporation of the liquid from the skin surface, leaving a residue of protective and drying powders. Lotions vary from unstable suspensions which must be shaken before application, to elegantly formulated oil-in-water preparations to which have been added agents which maintain the complex in suspension. Active principles of medication may be compounded in the lotion by the pharmacist or obtained in prepared formulations, as is also true of creams, which are generally water-washable, non-staining, semi-solid oil-in-water emulsions.

As continued use of these preparations may be drying, the lubricating ointments, such as water-in-oil emulsions or inert oils, are more appropriate to the dry, scaling and thickened chronic conditions, with the exceptions noted earlier. These occlusive ointments lubricate by retarding water loss from the skin, which is the major factor resulting in dryness of the skin, and are ordinarily obtained from a variety of sources including animal (lanolin, etc.), vegetable (corn oil, etc.), mineral (petrolatum, etc.) and synthetic derivatives.

Active (therapeutic) medications can be added to the lotion, cream and ointment vehicles as with antiinflammatory agents (corticosteroids, tars, etc.), antibacterial compounds (bacitracin, etc.), and antipruritic substances (menthol, phenol, camphor, etc.).

Recently, a number of newer vehicles have become available. While these in no manner reduce the value of the older vehicle-medication complexes, they do offer a greater degree of therapeutic versatility, relating in part to their potential use in all stages of the cutaneous inflammatory process. They include cooling topical pharmaceutical aerosol preparations, into which have been incorporated a number of dermatological medications in the form of solutions, suspensions, emulsions, powders and semi-solid substances. This pressurized propellant-solvent-medication mixture also has the advantage of being difficult to contaminate in the dispenser delivery system which is employed. Further, prepared solutions utilizing propylene glycol as a vehicle have enjoyed increasing popularity. In addition to its humectant, hygroscopic, solvent and preservative properties, propylene glycol offers considerable cosmetic advantage due to its clear, colorless, slightly viscous and nearly odorless nature. Cosmetically elegant lotion and cream vehicle formulations are also now available, varying from colorless liquids to creamy and pleasant to use oil-in-water emulsions with mildly lubricating, moisturizing capabilities, in contrast to the desired drying effects of the traditional shake lotion. Finally, semi-solid, clear, jelly-like suspensions in gel form serve as vehicles for a variety of topical medications, with a wide range of therapeutic indications.

Over the past several years, a number of new topical preparations have become available. Many of these utilize the newer vehicle formulations cited above, while others employ more traditional vehicles in a new medication-vehicle complex. A number of these preparations are presented in Table 2, which makes no attempt to compile an exhaustive list, but rather to provide a glimpse of those which offer considerable therapeutic potential. Among the more exciting of these recently developed medications are those which may offer lubrication-emollient characteristics for patients with chronic dry skin disorders, without the necessity for the greasy ointment preparations of the traditional type. A simple, hygroscopic, colorless, crystalline substance, urea, is now available in newer cream and lotion formulations, with or without hydrocortisone additives. This non-antigenic, non-toxic chemical enhances the water content of the skin on topical application, and has keratolytic, bacteriostatic, fungistatic, and antipruritic properties as well. This may reduce the need for the often cosmetically objectionable application of oils and ointments. Some patients do complain of a mildly disagreeable odor, however, coupled with stinging or burning sensations on application to dermatitic or fissured skin. Very recently, a gel composed of salicylic acid, propylene glycol, ethyl alcohol and water may provide partial alleviation in severe, genetically pre-determined ichthyoses, particularly when used with hydration and/or occlusion. Both types of preparation may have significance in the treatment of skin disturbances characterized by the presence of hyperkeratosis, as is found in keratodermas and callosities, for example.

Propylene glycol is the vehicle for the liquid form of vitamin A acid, which offers considerable benefit in mild to moderate comedonal and pustular acne, and for 5-fluorouracil solution, a fluorinated pyrimidine antimetabolite of proven value in the treatment of single or multiple actinic keratoses. This latter medication also has the capability to seek out and destroy clinically inapparent, early actinic keratoses, and thereby has potential prophylactic benefit as well.

The incorporation of corticosteroid in a surgical occlusive tape provides a convenient mode of application of this medication to localized chronic cutaneous disorders, utilizing the greatly enhanced penetration of the steroid which occurs under polyethylene film occlusion. Convenience of application is also found in the nightly use of selenium sulfide shampoo in the treatment of tinea versicolor, which offers considerable therapeutic efficacy as well. Ease of application and efficient photoprotection in the sunburn spectrum is available in alcoholic solutions of para amino benzoic acid, which are substantive to the skin to a greater degree than other sunscreen agents. This colorless solution may temporarily stain clothing, but with regular prophylactic use offers considerable promise in minimizing the sun-induced cutaneous changes which may lead to the development of premature wrinkling, aging and tumor formation in the predisposed individual, and the prevention of sunburn with allowance of tanning in the occasional user. Many of the other topical preparations listed in Table 2 could be cited in similar fashion.

TABLE 2

Topical Preparation	Condition(s)
Steroid cream or ointment (with polyethylene film occlusion)	Psoriasis Chronic eczematous disturbances
Steroid tape	Localized psoriasis Chronic eczematous disturbances
High concentration steroid creams	Localized psoriasis Localized eczematous disturbances Discoid L.E.
Steroid aerosol sprays	General topical steroid use Discoid L.E. Nickel jewelry contact dermatitis-on the skin and on the jewelry
Tolnaftate Haloprogin	Superficial dermatomycoses
Bleaching creams (hydroquinones, primarily)	Hyperpigmentary conditions
Topical nitrogen mustard	Mycosis fungoides
Proteolytic enzyme debridement	Necrotic soft tissues
Salicylic acid-propylene glycol-ethyl alcohol	Ichthyotic conditions Hyperkeratotic disorders
Psoralens with black light	Vitiligo
Sunscreen preparations (P.A.B.A.)	Conditions requiring protection against sunlight
5-Fluorouracil	Multiple actinic keratoses Xeroderma pigmentosum Basal cell tumors Bowen's disease Keratosis follicularis
Oxidizing acne lotions and creams	Acne
Vitamin A acid	Acne (also steroid-induced and pomade acne) Psoriasis Pityriasis rubra pilaris Ichthyotic conditions Keratosis follicularis Senile comedones Pseudofolliculitis of beard area of neck Nevus comedonicus
Gluteraldehyde	Hyperhidrosis Warts Fungal infections of nails
5-Iodo-2-deoxyuridine	Herpes simplex
Urea	Xerotic conditions Hyperkeratotic disorders
Selenium sulfide shampoo	Tinea versicolor
Acridine dyes (neutral red and proflavine)	Herpes simplex
50% aquaous propylene glycol solution with polyethylene film occlusion	Ichthyotic conditions
Aerosol sprays, solutions, gels, lotion formulations	Vehicles for topical medications for many dermatoses

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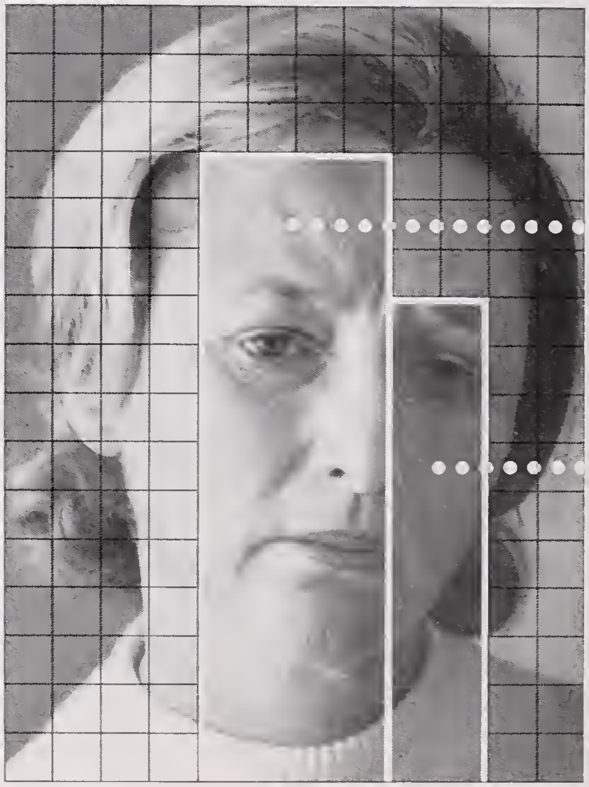
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and/ or severity of grand mal seizures
require increased dosage of standard
convulsant medication; abrupt withdra
may be associated with temporary increase in frequency and/ or severity of
seizures. Advise against simultaneous
gestion of alcohol and other CNS depre
sants. Withdrawal symptoms (similar
those with barbiturates and alcohol) h
occurred following abrupt discontinua
(convulsions, tremor, abdominal and
cle cramps, vomiting and sweating). K
addiction-prone individuals under car

respond to one

According to her major
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is is because her problem,
hough primarily one of ex-
ssive anxiety, is often accom-
nied by depressive symptom-
ology. Valium (diazepam)
n provide relief for both—as
excessive anxiety is re-
ved, the depressive symp-
ns associated with it are also
en relieved.

There are other advan-
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nagement of psychoneu-
ic anxiety with secondary
pressive symptoms: the
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lium is pronounced and
oid. This means that im-
ovement is usually apparent
the patient within a few
ys rather than in a week or

two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

For further information on this subject, the following references are provided:

1. Henry BW, *et al: Dis Nerv Syst 30*:675-679, Oct 1969.
2. Hollister LE, *et al: Arch Gen Psychiatry 24*:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics 11*:438-441, Sept-Oct 1970.

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in psychoneurotic
anxiety states
with associated
depressive symptoms

veillance because of their predisposi-
n to habituation and dependence. In
gnancy, lactation or women of child-
aring age, weigh potential benefit
inst possible hazard.
cautions: If combined with other psy-
otropics or anticonvulsants, consider
efully pharmacology of agents em-
yed; drugs such as phenothiazines,
cotics, barbiturates, MAO inhibitors
l other antidepressants may potentiate
action. Usual precautions indicated in
ients severely depressed, or with latent
ression, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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President's Letter

Oh! for the Simple Life

The Minnesota State Medical Association has been made dramatically aware of the kind of unilateral action that can occur in a bureaucracy. Much to the surprise of the Association, the Minnesota Department of Public Welfare (DPW) announced in late August that central billing of welfare claims was to begin on September 1. It further required that the billing be done on DPW Form 1497. The Medical Service Committee had been meeting with representatives of the Department of Welfare for several months, and negotiation on the forms still seemed to be in progress. DPW's sudden announcement produced a flood of irate calls to the State Medical Office, both from individual practitioners and from large clinic groups.

While the insurance industry, AMA, and the Social Security administration were attempting to simplify billing procedures, the Department of Welfare had drawn up a new and complicated form. This new form demanded eleven items of information not required by private insurance companies or Medicare.

Much of this additional information was necessitated by the optical scannable nature of Form 1497. We have determined that the State of Michigan, with the use of the computerized optical scanner, is paying bills promptly while the State of Ohio, using manual input, is two months behind in payments. So with some 20,000 welfare billings a day expected from physicians, dentists, pharmacists, hospitals, and nursing homes, the optical scannable form seemed a reasonable solution.

Given the necessity of a scannable form it seemed vital to develop a workable system, since central billing may well carry over into any National Health Insurance Plan. Many meetings were held in the next few days. After initial resistance and disbelief, the Welfare Department grasped the seriousness of the problems arising from the billing change. All parties agreed that nothing could be gained by a confrontation resulting from disagreement on billing practices.

Much of the information demanded on the form will not be mandatory, and the form seems workable if demands for more information are not added at a later date. We have asked that any demands by HEW for additional information be directed to the State Medical Office directly without the DPW as an intermediary.

Personally, I was very impressed with the ability and cooperation of the Department of Welfare staff. I was, on the other hand, disturbed by the ponderous bureaucratic machine and frightened by the possibility of its fifty-fold expansion under National Health Insurance.

As a result of these discussions between the Department of Welfare and the State Medical Association we have clarified our position and improved communications. We hope to avoid such emergency situations in the future.

Our goal with any government agency is to develop cooperatively a medical policy, not to react with crisis decisions.

Bernard Hall M.D.

President
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RNA Virus Associated with Human Transitional Cell Cancers of the Urinary Tract

ELWIN E. FRALEY, M.D.*; ARTHUR Y. ELLIOTT, Ph.D.;
PATRICK CLEVELAND, Ph.D. and NELL STEIN, M.S.

Evidence is presented that there is an RNA virus associated with human transitional cell carcinomas of the urinary tract. This agent resembles in some ways RNA viruses known to cause animal tumors.

There exists in almost every species of lower animals a group of RNA viruses which cause leukemia, sarcoma, and breast cancer. Furthermore, recent studies have implicated similar viruses as causes of sarcomas and breast cancer in sub-human primates. Irrespective of the species of origin or the type of malignancy which these viruses cause, all have certain shared characteristics. For example, the oncogenic RNA viruses have similar ultrastructure, a buoyant density of approximately 1.16-1.18 g/ml, all have RNA-directed DNA polymerase enzyme (reverse transcriptase) and the RNA 'core' of these viruses is made up, at least in part, of single-stranded, high molecular weight (70-80S) RNA. In addition, these viruses mature by budding through the cell membrane, and as far as is known, the only disease which they cause is malignancy. In that oncogenic RNA viruses from different species resemble each other in many ways, they are often referred to by the imprimature 'oncornaviruses.'

Because the viral causation of malignancy is so widespread in nature, scientists reasoned that viruses also probably cause a variety of human cancers. Furthermore, workers in this field assumed, based on the findings in lower animals, that the first human virus to be isolated would be an RNA virus and that this agent would be obtained from a leukemia, sarcoma, or breast cancer. As it turns out, at least the first of these assumptions probably was incorrect. The virus which now seems quite clearly to play a role in the pathogenesis of human malignancy is the Epstein-Barr (EB) virus, a DNA virus. In fact, the evidence that the EB virus causes a variety of lymphoproliferative disease including Burkitt's lymphoma is, in our opinion, incontrovertible. By contrast, massive efforts to identify a human oncornavirus-like agent from a variety of human cancers has met with little success. This paper summarizes briefly an attempt to isolate and characterize an oncornavirus-like agent from human transitional cell cancers of the urinary tract.

Virology of Human Transitional Cell Cancers (TCC) of the Urinary Tract

The collecting system of the human urinary tract is lined by a transitional epithelium from the calyces of the kidney to the proximal urethra. This epithelium often is referred to by the generic term urothelium. Transitional cell cancer may develop at any anatomic level, but tumors of the urinary bladder are the most common. Cancer of the bladder is an important clinical problem since this neoplasm accounts for approximately four percent of all human malignancies. An update concerning the important clinical aspects of bladder cancer has been prepared by us for Minnesota Medicine.

During the last four years we have examined in detail over 40 TCC of the human urinary tract by morphological, virus isolation and immunologic techniques for evidence of an associated virus. Both original surgical specimens as well as tumor cells growing in tissue culture have been studied.[1,2]

Examination of the original surgical specimen has shown these tumors consistently contain virus-like particles (VLP) and that the particles are of two different types morphologically. One of the two different particles which is seen most commonly in these tumors has an electron-dense central nucleoid which is surrounded closely by an outer or trilaminar unit membrane. The diameters of these VLP vary from 30 to 130 nm but the majority are 40 to 80 nm. The second less commonly found type of VLP has the nucleoid set apart from the unit membrane by a 5-10 nm less electron dense region and these particles have a diameter of 70-130 nm. These particles resemble morphologically the oncornaviruses which, as mentioned previously, cause a variety of animal neoplasms. Similar particles have not been found by a thorough search of normal uroepithelium, normal adult and embryonic kidney and renal adenocarcinomas (hypernephromas). The morphology of the VLP found in TCC is illustrated in Figure 1.

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Transitional cell cancer cell lines have been grown in the laboratory as continuous cell culture. Of course, all of these lines were established from fresh surgical specimens obtained directly from the operating room. One cell line designated 253J was derived from a retroperitoneal metastasis in a man with multiple TCC of both renal pelves, both ureters and the urinary bladder. The 253J cell line has been characterized in detail:[3] other TCC cell lines with which we have been working resemble closely 253J. In brief, all of the TCC cell lines have the following characteristics: (1) rapid growth, (2) epithelial morphology, (3) abnormal human karyotypes, (4) the ability to produce epithelial tumors in immune-suppressed animals, and (5) most of these cell lines produce virus-like particles which can be concentrated from the culture fluids in which the cells are propagated. These cells have been used in a variety of immunologic studies that are described herein and the results of these investigations suggest that these cells originated from human transitional cell cancers.[3,4]

After the TCC cells were established in culture, it was possible to grow them in large quantities and to harvest virus-like particles from the nutrient tissue culture fluids in which the cancer cells were grown. Virus-like particles coming from two different TCC cell lines have been concentrated using the technique of continuous flow centrifugation and PEG-pronase* as described elsewhere.[2] Once the particles were concentrated, they were characterized and it was shown that the human transitional cell cancer associated virus resembles closely RNA viruses known to cause tumors in animals as summarized in the Table. Again, the details of these experiments have been published.[2]

Immunological studies on chemically-induced tumors in animals have shown that, for the most part, these neoplasms possess tumor-associated antigens unique for each neoplasm. That is, chemical tumors contain antigens different from any other chemical tumor even if that other tumor is induced by the same carcinogen, in the same tis-

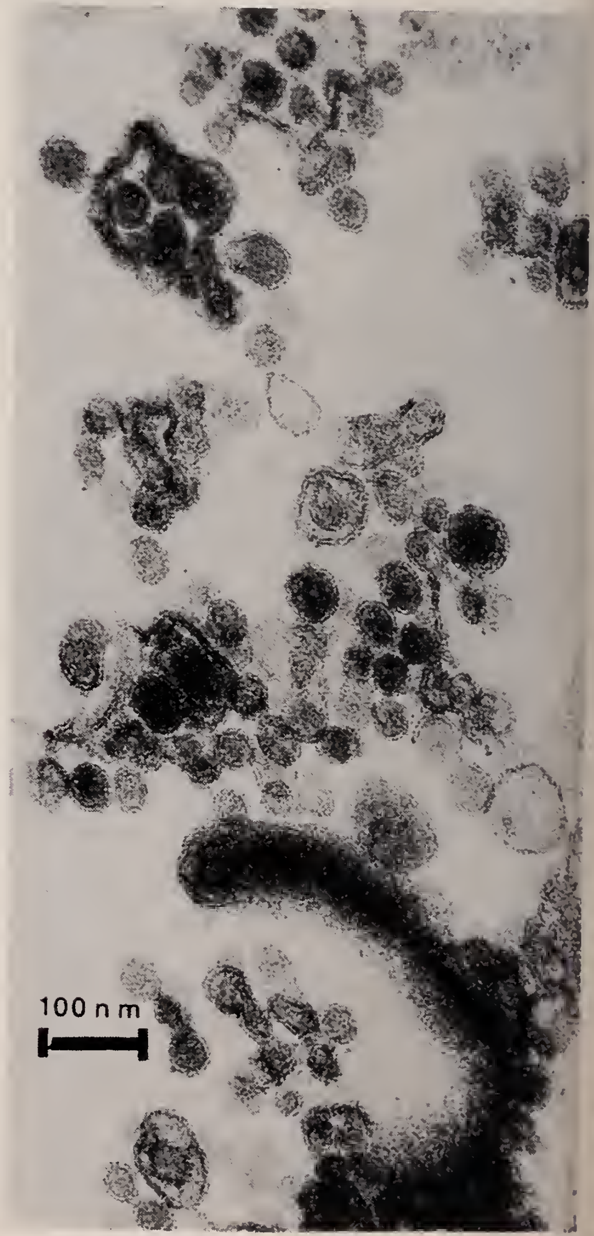

Fig. 1—Electron micrography of virus-like particles in a degenerating human transitional cell cancer cell (253J) in tissue culture. Both morphological types of virus-like particles which have been found in association with human transitional cell cancer of the urinary tract are seen. (X117,000).

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*PEG-pronase chemical used to purify viruses by removing cell debris from virus containing preparations.

sue-type and in the same animal. By contrast, the tumor associated antigens of virus-induced animal neoplasms are identical in all tumors produced by the same virus. Reasoning from these findings in the laboratory, if at least some human TCC are virus-induced, these tumors should possess common, unique cross-reacting tumor-associated antigens. Studies by Hakala et al,[4,5] using the in vitro lymphocyte-mediated microcytotoxicity assay and experiments by others[6] using the indirect immunofluorescence technique suggest that the TCC cell lines developed in our laboratory have common, unique, cross-reacting tumor-associated antigens. Thus, the immunological studies on human TCC to date are consistent with a viral etiology for these tumors. The finding that the sera and the lymphocytes from TCC patients react preferentially against our TCC cell lines suggests that these cell lines are indeed human TCC cells.[3,4,5]

Having established that there is an oncornavirus-like agent associated with TCC, we next examined whether the TCC associated virus (TCCAV) had oncogenic potential. In other words, could this agent cause normal mammalian cells including urothelium to 'transform' into malignant cells. To prove this, TCC tissue culture fluids were harvested, clarified to remove whole cells and cell debris and the clarified fluids were passed through an ultrafilter (0.45 mμ Millipore filter) which does not pass cells, but which is permeable to viruses. Next, the ultrafiltrates of the TCC culture fluids containing TCCAV were used to produce in vitro neoplastic transformation of mammalian cells—adult human testicle, human embryonic foreskin and embryonic calf urothelium. The cells transformed by the ultrafiltrates of TCC tissue culture fluids grew rapidly, ap-

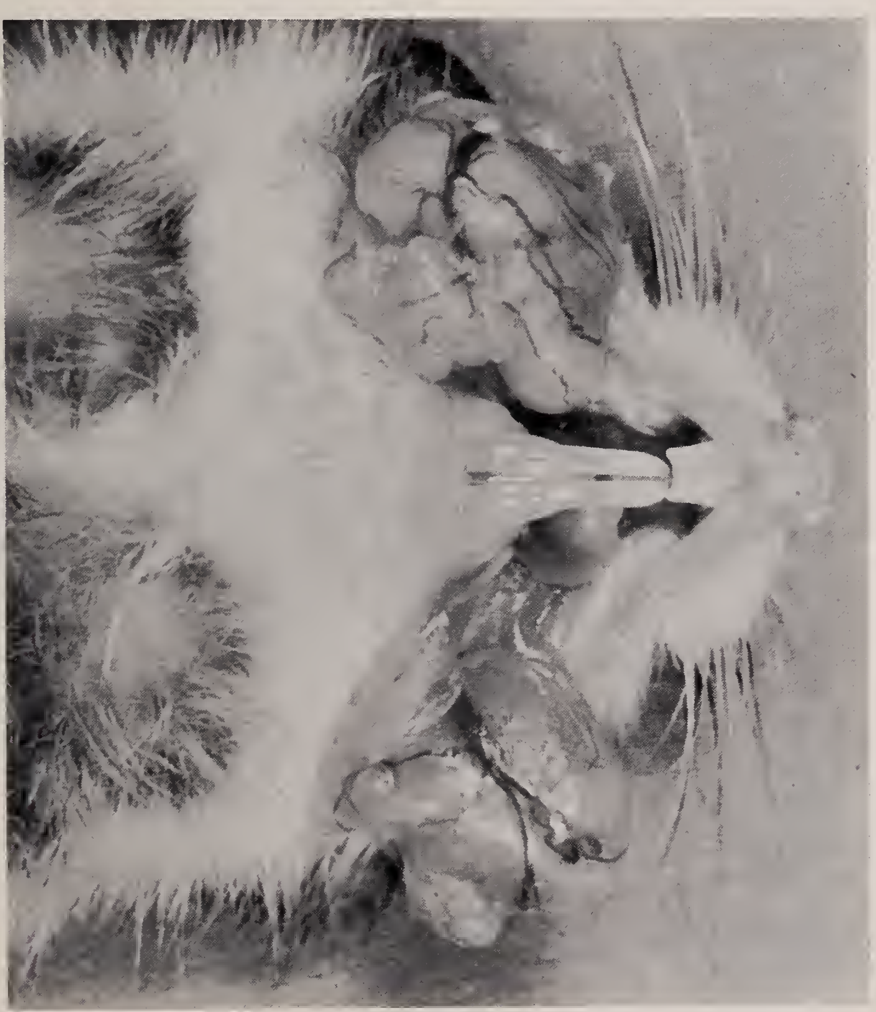

Fig. 2—Bilateral hamster cheek pouch tumors produced by injecting cells transformed by acellular tissue culture fluids from human transitional cell cancers as described in the text.

peared malignant, had abnormal human chromosome karyotypes, produced tumors in heterologous hosts (Figure 2), and the transformed cells had virus-like particles similar to the particles seen in TCC surgical specimens and in TCC cells in culture. In addition, the particles were similar to those concentrated and characterized from the TCC culture fluids.[2] Thus, the cells which were made 'malignant' by ultrafiltrates of TCC culture fluids, resembled cultured human TCC cells. Also, the transformed cells have antigen(s) that is recognized preferentially by the serums of TCC patients using the indirect immunofluorescence test.[3,6] This last finding suggests that, coincident with 'in vitro' neoplastic transformation produced by TCC culture fluids, antigen(s) appears on the transformed cells which is similar to the antigens of human TCC. Although we believe that this neoplastic transformation was produced by the TCCAV, transformation has not yet been produced by highly-purified virus preparations.

Discussion

It now seems that there is an RNA virus associated with human transitional cell cancers of the urinary tract. This virus resembles closely viruses known to cause neoplasms in animals. Further, there is evidence that the transitional cell cancer associated virus (TCCAV) is oncogenic, since it probably causes 'in vitro' neoplastic transformation in mammalian cells. We do not believe that this virus is simply a 'passenger' in these tumors because the agent is not one of the common infectious viruses of man and, as far as can be determined, the agent is not found in other genitourinary tumors. It is unlikely that a series of human tumors would each have the same unique virus consistently associated with them by chance.

Even though there is suggestive evidence that the TCCAV may cause TCC, to prove this point in the most pristine scientific sense is impossible. Koch's final or fourth postulate is that an organism suspected of causing a disease should produce the disease when injected back into the host from which it was originally isolated. This type of experiment cannot be carried out with the TCCAV or, in fact, with any other suspected human cancer virus for obvious reasons. Nevertheless, other current studies should provide at least additional circumstantial evidence as to whether the TCCAV is important in the pathogenesis of human urothelial tumors. For example, large numbers of tumors are being studied by morphological and virological techniques previously mentioned herein to determine if the majority of TCC of both the proximal and distal urinary tract have an associated virus. In addition, other experiments are examining whether the nucleic acid and virus-associated proteins of TCCAV share any homology with the nucleic acids and proteins of known oncogenic viruses. A major advance in the field of viral oncology in the past five years has been the development of sensitive radioimmune assay techniques to differentiate between avian, murine, feline and primate oncogenic viruses on the basis of the antigenic differences between their internal viral proteins. By applying these techniques to TCCAV it should be possible to tell whether TCCAV is a new virus or whether it is a known animal virus. Of course, if TCCAV is proven to be a new and unique agent closely related to but not identical with the primate oncogenic RNA viruses, this will strengthen the possibility that TCCAV is indeed

TABLE
COMPARISON OF TCCAV AND ONCORNAVIRUSES

	TCCAV	Known RNA Tumor Viruses
Size (diameter)	40-130 nm	80-120 nm
Found in Tumors	+	+
Reverse Transcriptase	+	+
RNA Predominates Nucleic Acid	+	+
Buoyant Density	1.14-1.18g/ml	1.16-1.18g/ml
Morphology	Dense Nucleoid With Unit Membrane	Dense Nucleoid With Unit Membrane
High Molecular Weight RNA (70-80S)	+	+
Matures By Budding Through Cell Membrane	?	+
Presence of GS Antigen	Suggested*	+

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*Preliminary data.

a human tumor virus.

There are at least three practical implications of the virus association with human TCC-UT. First, it should be possible to develop a highly-specific screening or cancer detection test for these tumors. Such a test may be useful irrespective of whether the virus actually causes TCC-UT since the virus is found consistently in the tumors, and because the sera of most tumor patients contain antibodies that recognize virus or virus-directed antigens. Second, since TCC cells and cells transformed by TCC tissue culture fluids appear to share common, tumor-specific antigen it might be possible to develop antisera to this antigen that could be used in the indirect immunofluorescence technique to detect malignant exfoliated cells in the urine. The use of immunocytology should improve the accuracy and sensitivity of diagnostic urinary cytology. Third, chemoprophylaxsis may be able to control early tumors. This postulate is based in part on the studies showing that a variety of drugs interfere with virus replication and the transforming capacity of the oncornaviruses. If antiviral chemotherapy were administered on a continuing basis to patients early in the course of their disease, tumor recurrences and the progression of benign to more malignant tumors might be obviated. However, before such a chemotherapeutic approach is tried, the many nuances of this virus-tumor system require greater understanding and better methods for assessing the status of TCCAV infection in patients must be developed.

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Sometimes weak and confined to bed at others stronger and sanguine, Gertrude Fulford was passing along the dark and troublous path whereby consumption drags its victims to their graves . . . It was one of those rapid cases which (although, perhaps, the insidious enemy may have been surely working for a long time) declare themselves after they have become next to hopeless, and then hurry on to the catastrophe. Gertrude knew at last that she was to die; but the end did not then seem so near as it was. She lay on the sofa: she had been talking cheerfully, and at last asked to be moved to her room; when the room was reached she had fainted. This swoon was the first of a series which continued at intervals until she at last passed from her trance into eternity.*

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*W. G. Hamley, Disorder in Dreamland. Blackwood's Edinburgh Magazine, 1874.

Hennepin County Academy of Family Physicians

The Hennepin County Academy of Family Physicians is sponsoring the Annual Invitational Banquet. A social hour at 6:00 P.M. in the Garden Court of the Radisson South Hotel, with dinner scheduled at 7:30, on Thursday, November 21, 1974. Entertainment for the evening will be Bob Hudson and Ron Landry, recording artists of multifaceted talents as exemplified with their first two Albums *HANGING IN THERE* and *LOSING THEIR HEADS*. Information on tickets contact Alan K. Schultz, M.D., at 537-8853 (Area Code 612), or 5920 Kirkwood Circle, Minneapolis, Minnesota 55442.

California (La Crosse Virus) Encephalitis

in Minnesota

HENRY H. BALFOUR, JR., M.D.*

California encephalitis (CE) in Minnesota is caused by the La Crosse virus, which has been isolated from adult mosquitoes collected in Winona and Carver Counties. Epidemiologic studies indicate that areas of La Crosse virus activity may be very localized. CE has been documented in 83 children hospitalized in Minnesota during the summers of 1967 through 1973. All the patients survived, but 15% had sequelae. A mild and a severe clinical form of CE were defined, with the severe form becoming more prevalent during the last three years. A recently developed counterelectrophoresis test can provide early and rapid diagnosis in 38% of cases.

CALIFORNIA ENCEPHALITIS (CE) in Minnesota is caused by the La Crosse virus, a mosquito-borne agent belonging to the California group of arboviruses.[1] CE has been documented in 83 children hospitalized in Minnesota during the summers of 1967 through 1973. It is the second most common form of summertime viral meningoencephalitis in our area. Only the enterovirus group is responsible for more viral central nervous system (CNS) infections during the summer months. This is a discussion of the history and epidemiology of CE in Minnesota and a description of the clinical and laboratory findings during the acute illness.

History

In September, 1960, a four-year-old girl from Dresbach, Minnesota died of meningoencephalitis in Lutheran Hospital, La Crosse, Wisconsin. Virologic tests performed at the time were negative, but portions of brain tissue were preserved at –40°C at the State Laboratory of Hygiene, Madison, Wisconsin. A serologic survey which was completed in 1964 indicated that human infections with California arboviruses occurred in Wisconsin.[2] The brain tissue was then restudied and a California arbovirus was isolated in suckling mice.[3] The agent was designated as La Crosse virus, and this has been the subtype of the California arbovirus group responsible for most cases of CE in the United States.[4]

Although the first recognized case of CE in Minnesota occurred in 1960, additional Minnesota cases were not reported to the National Center for Disease control until 1965.[5] Johnson and Rodgers described the first series of Minnesota CE patients in 1967.[6] Since 1967, the virus laboratory of the Minnesota Department of Health has routinely tested sera from patients with acute summertime CNS infections for evidence of CE. A total of 83 patients has been identified during the period 1967 through 1973 (Table 1).

TABLE 1
Distribution of California (La Crosse Virus) Encephalitis by Years

Year	Cases of CE
1967	8
1968	5
1969	9
1970	15
1971	18
1972	11
1973	17
TOTAL	83

From the Departments of Laboratory Medicine, Pathology, and Pediatrics, University of Minnesota Medical School, and the Division of Medical Laboratories, Minnesota Department of Health.

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Epidemiology

CE has been exclusively a pediatric disease in Minnesota. All of the 83 patients were children between the ages of six months and 17 years. Forty-seven (57%) of the children were in the five-to nine-year-old age group.

CE is the second most common form of laboratory-documented viral meningoencephalitis in Minnesota during the months of June through September. CE was serologically confirmed in 7.1% (83/1162) of patients with acute CNS infections tested during the summers of 1967 through 1973. During that same period, enteroviruses accounted for 20% of cases, mumps for 5.3%, *Herpesvirus hominis* for 2%, and viral agents were not detected in 64%.

The age-related incidence of CE is shown in Table 2. Younger children are most commonly affected, especially those between the ages of five to nine years. Approximately one out of every five Minnesota children in the five-to nine-year-old age group with a summertime CNS infection had CE.

La Crosse virus was the California subtype responsible for CE in all of the Minnesota patients appropriately tested.[7] Epidemiologic studies in both Minnesota and Wisconsin have implicated the *Aedes triseriatus* mosquito as the principal vector for La Crosse virus.[4,8] This mosquito prefers to breed near water in the basal holes of hardwood trees.[9] It does not ordinarily fly very far from its deciduous forest breeding sites.[10] Its natural hosts are small woodland animals such as squirrels and chipmunks (Figure 1). These animals can act as an amplification system during their period of viremia. Uninfected mosquitoes feed on the viremic animals and acquire the virus. These mosquitoes may then infect other animals or humans.

Once the La Crosse virus is found in a particular area, it tends to remain there in subsequent years. Until very recently, the overwintering site of La Crosse virus was not known. Data from Wisconsin now indicate that transovarial passage of the virus occurs and that infected adult mosquitoes deposit infected eggs in basal tree holes (Figure 1). The La Crosse virus overwinters in infected eggs and/or larvae and hence some of the adults that hatch the following spring harbor

TABLE 2
Incidence of California (La Crosse) Encephalitis by Age Groups, 1970-1973

Age Group	No. With Acute CNS Disease	No. With CE	Percent With CE
0-4 years	170	19	11.2
5-9	149	32	21.5
10-14	113	9	8.0
15-19	98	1	1.0
20+	372	0	0.0
Totals	902	61	6.8

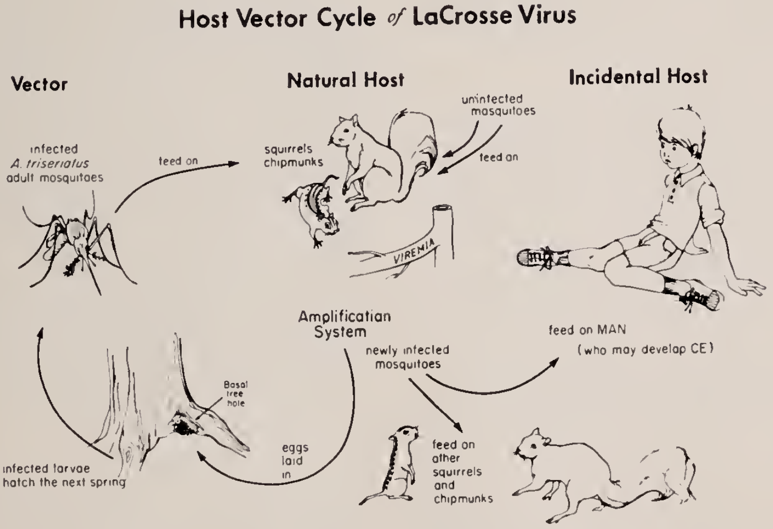
Host Vector Cycle of LaCrosse Virus
Vector
Natural Host
Incidental Host
infected A. triseriatus adult mosquitoes
feed on
squirrels chipmunks
uninfected mosquitoes
feed on
VIREMIA
Amplification System
newly infected mosquitoes
feed on MAN (who may develop CE)
Basal tree hole
eggs laid in
infected larvae hatch the next spring
feed on other squirrels and chipmunks

Fig. 1—The host-vector cycle for La Crosse virus. Infected mosquitoes normally feed on small animals who act as an amplification mechanism for virus spread. Uninfected mosquitoes feed on viremic animals and acquire virus. They may then transmit it to other animals or man. Recent evidence indicates that La Crosse virus is passed transovarially and overwinters in eggs or larvae.

infectious viruses.[11] Studies are currently underway in Minnesota to evaluate this overwintering mechanism.

The distribution of CE by counties is shown in Figure 2. Seventy-four patients were residents of Minnesota and nine lived in extreme southwestern Wisconsin; all were hospitalized in Minnesota. All of the patients were from rural or suburban areas.

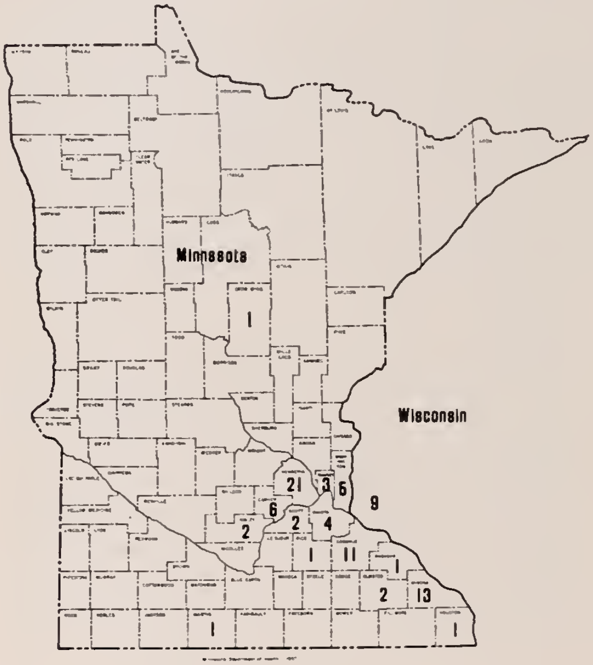

Fig. 2—Distribution of California (La Crosse) encephalitis by counties, 1967-1973. Nine of the 83 children hospitalized in Minnesota were from southwestern Wisconsin.

Until 1968, confirmed cases of CE were limited to the southeastern portion of Minnesota, where the ecology was ideal for *Aedes triseriatus*. A field study conducted in the Winona area in 1968 indicated that La Crosse virus could be isolated from *Aedes triseriatus* mosquitoes and that 27% of the population had neutralizing antibodies to La Crosse virus.[12] Thus, human infections with this arbovirus were prevalent in rural Winona. Fortunately, most of these infections were asymptomatic. Of 278 persons with antibody, a history of acute CNS illness was obtained in only four children (1.4%).

Since 1968, there has been an apparent northwestward migration of CE, and cases have been recognized with increasing frequency in the western suburbs of Minneapolis. In 1970 for example, five of the 15 cases of CE occurred in southwestern Hennepin and northeastern Carver Counties. Two of these five patients were neighbors who lived in Zumbra Ridge, a small residential peninsula in Carver County.

Epidemiologic studies have been conducted in Zumbra Ridge each year since 1971 in cooperation with Drs. Henry Bauer and Robert A. Siem of the Minnesota Department of Health and the late Albert W. Buzicky of the Metropolitan Mosquito Control District. The ecology of Zumbra Ridge was found to be similar to the Winona area. Hardwood trees were abundant and were situated near water. Three La Crosse virus strains have been isolated from 145 pools of adult mosquitoes. Two of the isolates were made from pools that contained *Aedes triseriatus* and one isolate was recovered from a pool of *Aedes vexans*. Over half the small animals tested (10/19) had antibodies to La Crosse virus, and 17% of the residents (16/91) had antibodies.[10] Of the 16 Zumbra residents with positive La Crosse antibody titers, 13 lived in one small sector of the community where hardwood trees were abundant, suggesting that foci of La Crosse virus activity may be very localized. If this finding can be confirmed in other areas, it might be practical to control CE by (1) frequent spraying to reduce the population of adult *Aedes triseriatus* and (2) filling in the basal tree hole breeding sites in the localized areas of virus activity. Virologic studies in a Hennepin County community near Zumbra Ridge are in progress to further define the geographic distribution of La Crosse virus.

Because *Aedes triseriatus* mosquitoes hatch late in the spring, CE does not occur until the latter part of June in Minnesota and ends in September when cool weather limits mosquito activity. The earliest date of onset of CE in Minnesota has been June 24th, and the latest September 28th. The incubation period is not known precisely. However, histories of heavy mosquito exposures in several of our patients indicate that the incubation period is short, ranging from three to seven days.

Four pairs of siblings have had CE (Table 3). This is not surprising since siblings would be likely to play in the same infected woodland areas. Although theoretically possible, it is highly unlikely that intrafamilial person-to-person spread of La Crosse virus occurs. The long intervals between the dates of onset in three of the sibling pairs militates against person-to-person infection.

TABLE 3
California (La Crosse) Encephalitis in Siblings

Initials	Age in Years	Date of Onset
1. DT	4	7/30/67
JT	2	8/28/67
2. TG	4	8/14/70
FG	7	8/30/71
3. DV	3	8/21/73
TV	1½	8/24/73
4. SD	4	8/25/73
ED	7	9/26/73

Clinical Findings

Two distinct clinical patterns of CE could be defined. The mild form of illness began with a two- to three-day prodrome of fever (38.5 to 39 C), headache, malaise, and gastrointestinal symptoms. The latter usually consisted of anorexia, abdominal pain, and vomiting; diarrhea was uncommon. About the third day the temperature increased (39.5 to 40 C), the patients became lethargic with evidence of meningeal irritation and were admitted to the hospital. Fever and CNS findings abated gradually during the next week. These patients were discharged without overt neurologic sequelae and without medication.

The more severe form of CE began abruptly with fever (39 C) and headache followed 12 to 24 hours later by the sudden onset of focal or generalized seizures. Such patients were rushed to the hospital where intensive supportive care was required. The initial seizure activity frequently was prolonged and difficult to control. The most effective anticonvulsant was parenteral diazepam (Valium). Clinicians in areas where CE is endemic believe that without rapid supportive care, including in certain instances assisted respiration, some patients with this form of CE would have died during the initial phase of illness. These patients were hospitalized for an average of 12 days and many required intravenous fluids for the first two to three days. All patients who had this severe form of CE were discharged on anticonvulsants. There were no fatalities.

The more severe form of CE became predominant in Minnesota during the last three years (Table 4). It is possible that local virus strains are becoming more virulent, but other factors, such as reluctance to submit specimens from patients who are not very ill, may be responsible for the apparent increase in severity of the disease.

Clinical Laboratory Findings

Peripheral white blood cell counts on admission ranged from 6,900 to 30,700/cu mm with a median cell count of 16,500 ($\bar{x} = 17{,}096$). The differential counts ranged from 54% to 96% polymorphonuclears with a median differential of 81% PMNs ($\bar{x} = 80$).

Fifty-eight (90%) of the 63 patients tested had cerebrospinal fluid (CSF) leukocytosis on admission but the counts were not high (median cell count = 47, $\bar{x} = 103$). The initial CSF differentials ranged from 98% polymorphonuclears to 98% mononuclear forms.

Electroencephalograms (EEGs) were abnormal in 26 of 27 children during the acute phase of CE. Generalized slow wave activity was the most frequent abnormality and was present in 10 patients. Localized slowing was found in eight children. Epileptiform activity was seen on two tracings.

Brain scans using ^{99m}Tc-pertechnetate were obtained in 11 patients, 10 of whom had severe illnesses. Four children had abnormal scans showing increased radioactive uptake in the right temporal region in two instances, in the right parieto-occipital area in one, and in the left parietal region in one. Considering both EEGs and brain scans, there was a predominance of right hemisphere involvement, and a predilection for localizing findings in the frontal and temporal regions.

Mixed Infections

Six of our patients have had mixed infections with La Crosse virus and other viral agents. Four children had dual infections with La Crosse and enteroviruses. One child had a dual infection with La Crosse and adenovirus type 1. A six-year-old girl, whose case has been reported in detail, had a triple infection with La Crosse virus,

TABLE 4
Yearly Distribution of California (La Crosse) Encephalitis by Type of Clinical Course

Year	Cases of CE	Mild Form	Severe Form	Clinical Data Insufficient
1967	8	6	0	2
1968	5	1	2	2
1969	9	4	3	2
1970	15	8	5	2
1971	18	7	11	0
1972	11	3	7	1
1973	17	7	10	0
Totals	83	36	38	9

echovirus 11 and mumps.[14] As a group, the children with mixed infections did not have a more severe clinical course than the other CE patients. Mixed bacterial and La Crosse infections did not occur.

Diagnosis

CE should be suspected clinically in a child, especially in the five- to nine-year age group, who develops meningoencephalitis during the months of June through September. A history of having been in a deciduous forested area during the preceding two weeks makes probability of CE even greater.

To confirm the clinical diagnosis, paired serum specimens are required. The first serum should be obtained as soon as possible after the onset of illness and the second should be collected three to six weeks later. The laboratory diagnosis is based upon a fourfold change in La Crosse hemagglutination-inhibiting, neutralizing, and/or complement-fixing antibodies. A detailed discussion of the antibody responses in CE has been presented elsewhere.[1,7]

Recent studies in our laboratory have indicated that a counterelectrophoresis test detected 38% of CE patients during their acute illnesses.[7,13] Since this test can be performed in two hours, it will enable us to make a rapid laboratory diagnosis in some patients. Rapid diagnosis is particularly important for CE patients who have focal findings resembling *Herpesvirus hominis* encephalitis, and thus might be subjected to a brain biopsy. Indeed, one Minnesota CE patient who had a right temporal lobe focus demonstrated by EEG and brain scan was biopsied because the clinical diagnosis was herpesvirus encephalitis.[1]

Differential Diagnosis

The severe form of CE, especially when focal findings are present, initially may resemble herpesvirus encephalitis. As Hilty et al.[15] have pointed out, patients with herpes deteriorate while those with CE show neurologic improvement after two to three days. Also, CE usually occurs in children between the ages of five to nine years, whereas herpesvirus encephalitis usually is found in persons less than one year old or older than 15 years. Hence, the age of the patient and the early clinical course may distinguish CE from herpesvirus encephalitis.

CE patients can have a relatively mild meningoencephalitis similar to that of enteroviral or mumps CNS infections. The epidemiology may be of assistance in the differential diagnosis, since both mumps and enteroviral meningoencephalitis tend to occur during community-wide epidemics. Also, if the patient has not been in a wooded area within the past two weeks, the diagnosis of CE is unlikely. Parotitis, if present, is virtually diagnostic of mumps. A rash is suggestive of enteroviral CNS infections, although one of our CE patients had a transient maculopapular truncal rash. Patients who present with the severe form of CE do not resemble the typical patient with mumps or enteroviral meningoencephalitis. Seizures and stupor are uncommon in mumps and rare in enteroviral infections. Also, if focal findings are present, mumps or enteroviral meningoencephalitis is quite unlikely. We have not found a report of a focal mumps or enteroviral CNS infection.

The initial peripheral leukocytosis and predominance of neutrophils in the CSF of some CE patients might cause one to suspect bacterial meningitis. However, the low CSF leukocyte count, normal glucose content, negative Gram stain and subsequent sterile culture rule out bacterial meningitis.

Sequelae

Follow-up data on 33 patients were obtained from one to five years after the acute illness. Five children (15%) were found to have sequelae. All five had had severe illnesses. The girl who had undergone a right temporal lobe biopsy during her acute illness had a mild paresis of the left arm. Four children had personality or behavioral problems such as emotional lability, excessive irritability, and inattentiveness in school. Six of eight follow-up EEGs were abnormal, showing excessive high voltage sharp and slow wave activity which was localized to the left side in two patients and to the right side in one.

Comment

California encephalitis was so named because the original strain of this group of arboviruses was isolated in California in 1943.[16] Unfortunately, the name is misleading because CE has not been confirmed in California since 1945. Indeed, the three states with the largest number of CE patients are Ohio, Wisconsin, and Minnesota.[5] It would be more appropriate to rename the disease La Crosse encephalitis, since the La Crosse virus has been responsible for almost all cases of CE in the United States.[4] The term CE has become so familiar that we have retained it in this report.

At present, CE is the second most common form of viral summertime CNS infection in our area. It is probable that increased surveillance by Minnesota physicians will result in the documentation of many more cases of CE than are currently being recognized. This hypothesis is supported by epidemiologic studies that have identified persons with symptomatic La Crosse infections who were not originally considered to have had CE.

Acknowledgment

Charlene K. Edelman and Sandra J. Pitt provided skilled technical assistance. Drs. Robert A. Siem and Henry Bauer made valuable suggestions. Mrs. Annette Scagnetti coordinated the epidemiologic studies in Zumbra Ridge.

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Recurrent Anterior Dislocation of the Shoulder

Surgical Repair with A Modified Bristow Procedure

PHILIP H. HALEY, M.D.* and JAMES H. HOUSE, M.D.†

This brief review of the current management of anterior shoulder dislocation is presented to emphasize proper treatment of primary dislocations, particularly to assure adequate immobilization.

ANTERIOR DISLOCATION of the shoulder has been recognized since antiquity. It is the most common dislocation and occurs in all age groups with males involved twice as frequently as females. Recurrent dislocation is common, particularly in young patients. The overall recurrence rate is 55 to 60% but in persons under the age of 20 the recurrence rate is nearly 90%. The young adults seen at the University of Minnesota Student Health Service have provided a population to study this injury and its treatment.

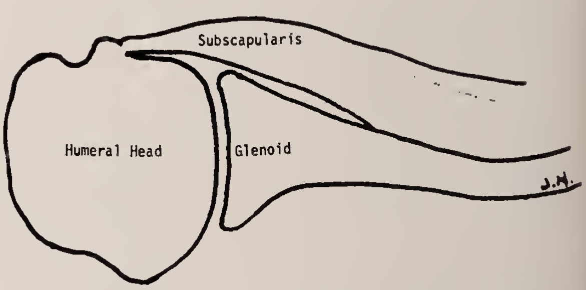

Fig. 1—Diagrammatic representation of cross section of shoulder joint including m. subscapularis. Note shallow glenoid compared to diameter of humeral head.

Pathomechanics

The glenohumeral joint is a shallow "ball and socket" joint, stabilized by the rotator cuff and a relatively lax capsule that allows a remarkable range of motion (Figure 1). The established patterns of injury are several: falling on or hyperextending an abducted arm, excessive external rotation in abduction, or a direct blow to the back of the shoulder. Certain pathological findings subsequent to anterior dislocation have been observed during surgery and others are visible on Xray. The glenoid labrum is detached from the bone and the anterior capsule is elevated from the neck of the scapula to form a large recess deep to the subscapularis muscle into which the humeral head dislocates (Figure 2). This is the Bankart lesion and is often revealed on Xray by the presence of small bone fragments avulsed from the glenoid rim. A bony defect consisting of flattening of the posteolateral aspect of the

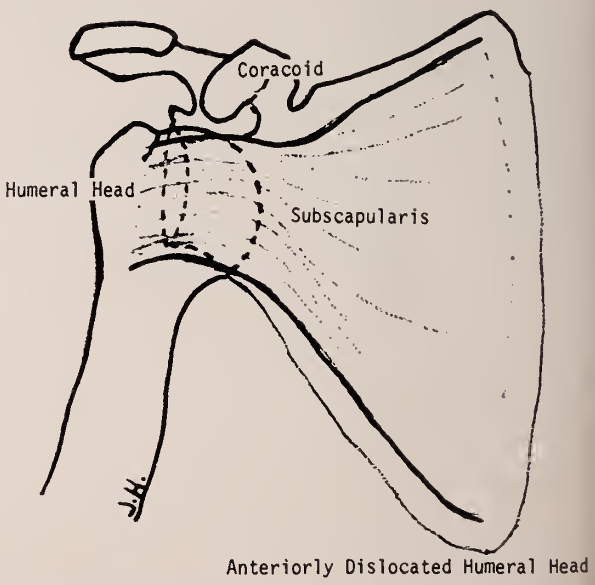

Fig. 2—Schematic representation of anterior view of dislocated shoulder showing humeral head displaced medially by retraction of subscapularis muscle.

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humeral head is found in many patients (Figure 3). This is the Hill-Sachs lesion that is demonstrated as a notch defect in the humeral head on an Xray taken in internal rotation. This bony defect predisposes to recurrent dislocation.

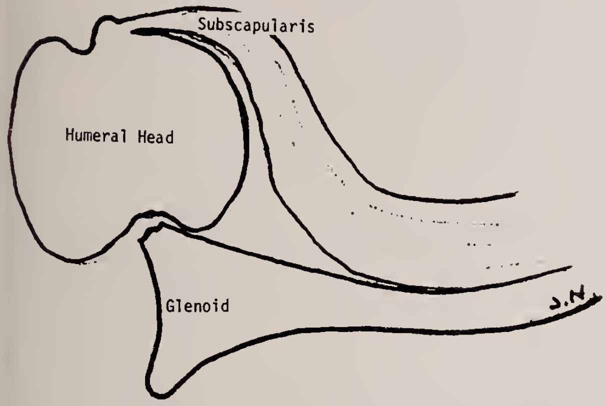

Fig. 3—Diagrammatic representation in cross-section of anteriorly dislocated shoulder.

Clinical Features

A dislocated shoulder is usually easily recognized. The patient typically holds the injured extremity in a slightly abducted and externally rotated position. Pain is obvious, and it is not possible for him to bring his hand to touch the opposite shoulder. Inspection shows the shoulder to have lost its rounded contour and palpation beneath the acromion confirms that the humeral head is displaced. Examination for deltoid muscle function and sensory loss of the mid-deltoid region should be routinely carried out prior to manipulation to evaluate for possible axillary nerve injury. Injury to other branches of the brachial plexus can occur with violent dislocations. Confirmation of the dislocation by Xray should be done prior to reduction to look for a fracture of the greater tuberosity which is often seen in older patients.

Primary Treatment

There are several methods of manipulation of the shoulder to achieve reduction. Analgesia and muscle relaxation are important adjuncts; occasionally, general anesthesia is necessary. The Hippocratic and Stimson methods are well known techniques of applying traction to the arm to obtain the passive lengthening or relaxation of the subscapularis muscle which is required to achieve reduction. The Kocher maneuver is rarely indicated and must be gently done to avoid further injury. In order to minimize the risk of recurrent dislocation in young adults the arm should be immobilized for three to four weeks to allow the capsule to heal. A shorter period is used for older persons who are more likely to develop stiffness. Proper immobilization in adduction and internal rotation can be easily accomplished with a sling and swathe, a Velpeau bandage, or a stockinette sling. Isometric exercises of the shoulder and arm can be done during the immobilization period. Thereafter circumduction and pendulum exercises are used to regain a full range of motion.

Recurrent Dislocation—Surgical Considerations

Recurrence usually requires a significant reinjury but each subsequent dislocation requires less force and some shoulders become so unstable that a simple maneuver such as combing the hair or reaching up to turn on a light may cause the shoulder to dislocate. The condition does not spontaneously improve although activity restriction and isometric exercises may reduce the frequency of recurrence. Surgical repair is necessary when work or sports participation requires abduction and external rotation of the shoulder and is strongly advised for patients with dangerous occupations such as a steel worker on tall buildings. Many operations have been proposed. Some are designed to limit external rotation, others involve ligament reconstruction, or tendon check-rein mechanisms. The essential element of many repairs is to tie down the subscapularis and promote the formation of a massive scar anterior to the joint thereby limiting shoulder motion and preventing dislocation.

A more dynamic concept for reconstruction was proposed by Bristow over 20 years ago but only during the past ten years has it become generally known. Various modifications have evolved, but the basic anatomical feature of this

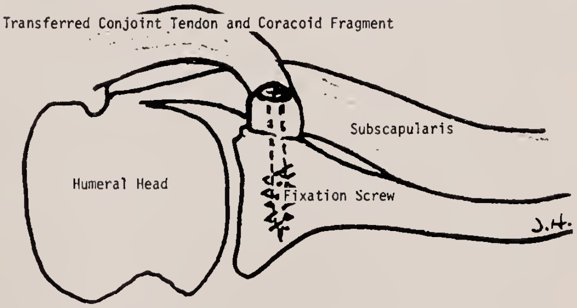

Fig. 4—Cross-section of shoulder joint showing coracoid process with the attached tendons of coracobrachialis and short head of biceps transposed to anterior glenoid.

procedure is that it provides both a bony block and a dynamic check-rein that prevents recurrent dislocation. The coracoid process is transposed to the glenoid neck to obliterate the anterior capsular recess while the attached tendons of origin of the short head of the biceps and coracobrachialis form a muscular sling that is effective in preventing the subscapularis from displacing anteriorly or superiorly as the limb is abducted and externally rotated (Figure 4). This repair is thus both statically and dynamically effective when the limb assumes the position of vulnerability, yet shoulder mobility is not sacrificed as it is in many other methods of repair.

Technique

The operation is no more difficult than "conventional repairs." A straight skin incision in a line from the coracoid process to the anterior axillary fold allows adequate exposure and yields a cosmetically acceptable scar even in females. The deltopectoral interval is developed to allow exposure of the coracoid process. The origins of the short head of the biceps and coracobrachialis muscles are defined on the tip of the coracoid and after pre-drilling the coracoid for a bone screw, about 1 cm. of it is detached with an osteotome just distal to the attachment of the pectoralis minor (Figure 5). After reflecting this fragment and its muscular attachments about three cm. (taking care to protect the musculocutaneous nerve) the exposed subscapularis muscle and its tendon are incised in line with its fibers about midway between its superior and inferior borders. (Figure 6). After dissecting the posterior surface of the subscapularis from the anterior capsule of the shoulder joint a self retaining retractor, such as the Millin-Bacon suprapubic retractor, is placed in the "buttonhole" opening in the subscapularis. This provides exposure of the scapular neck and glenoid rim.

The capsule at the glenoid labrum is incised in a T-fashion, the edges of the T are tagged with sutures and the underlying cortex of the scapula just medial to the glenoid margin is exposed. A hole is drilled through the cortex to receive the cancellous screw that is used to attach the coracoid and its tendons to the bone. The tagged flaps of the capsule are then sutured over the coracoid process further obliterating the recess (Figure 7). The division in the subscapularis is loosely closed around the transposed ten-

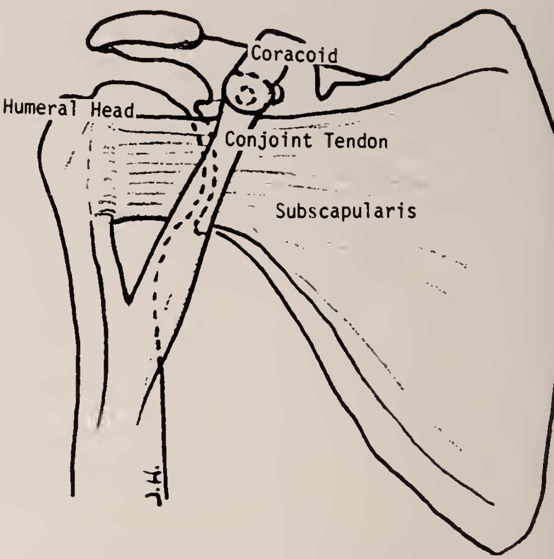

Fig. 5—This figure illustrates the anatomy of the anterior aspect of the shoulder joint prior to repair.

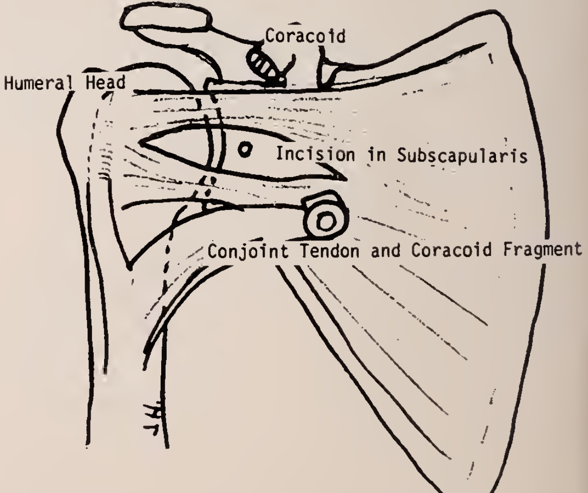
Coracoid
Humeral Head
Incision in Subscapularis
Conjoint Tendon and Coracoid Fragment
J.H.

Fig. 6—Illustration of incision in the subscapularis through which the coracoid is transposed.

dons to avoid dense scar fixation of the muscle that might limit shoulder motion. A suction drain is inserted and the wound is reapproximated in layers with absorbable suture. A subcuticular skin closure is used for cosmetic reasons.

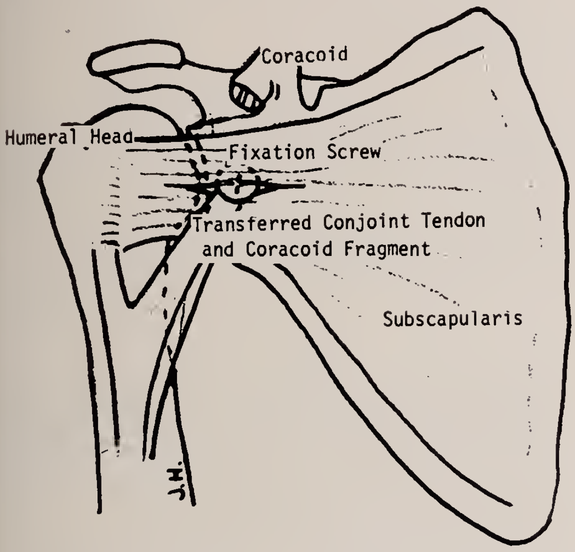

Fig. 7—The completed procedure with the coracoid process transposed through the subscapularis to the anterior aspect of the scapula.

Immobilization is by a stockinette Velpeau or a sling with a supplementary Ace bandage around the chest. The shoulder is kept immobilized four weeks after which a gentle rehabilitation program is begun using a sling part time for two more weeks. Lifting or forceful use of the biceps should be avoided for eight weeks to allow adequate healing of the coracoid to the neck of the scapula.

Results

Since 1965 more than forty such repairs have been done at the University of Minnesota Hospitals and the University of Minnesota Student Health Service. The consistently good functional results have been very encouraging. There have been no recurrences in this group of patients and little if any loss of motion has been noted on follow-up examination. Furthermore, no patient has had to make significant alterations in his employment or activity as a result of shoulder disability and many have returned to activities previously precluded by recurring dislocations.

Complications

Many of the patients in their enthusiasm to return to the activities have discarded their bandages earlier than advised. The only complication occurred in one patient who forcefully contracted his biceps muscle (grabbing a rock while floating down the Apple River only six weeks after surgery) and pulled out the coracoid screw but did not dislocate his shoulder. At the time of screw removal the repair was noted to be remarkably stable. No infections or musculocutaneous nerve injuries have occurred in this series. One serious complication has been reported in the literature. Loosening and displacement of the screw caused a false aneurysm of the axillary artery with subsequent brachial plexus compression and upper extremity paralysis. Functional improvement occurred after screw removal, exploration of the brachial plexus, and repair of the aneurysm.

Summary

When surgery for recurrent dislocations is indicated the modified Bristow repair is strongly recommended. This relatively new surgical procedure logically and dynamically corrects the pathomechanics of recurrent anterior shoulder dislocation. Our experience has confirmed that this procedure is effective in preventing recurrences while retaining shoulder motion and we expect that it will become more widely used in the future.

Renal Transplantation

At The University Of Minnesota

1968-1973

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S. M. MAUER, M.D.* B. von HARTITZSCH, M.D.* and J. S. NAJARIAN, M.D.*

This paper describes clinical transplantation methods as they have evolved over the last six years at the University of Minnesota.

ALTHOUGH RENAL TRANSPLANTATION has been performed at the University of Minnesota Hospitals since 1963, only since 1968 has kidney transplantation become one of our major clinical undertakings. The transplantation unit then formed is now the largest in the world.

Organization

A special ward of 23 beds, staffed as an intensive care unit, is used exclusively for transplantation and hemodialysis patients. Two staff surgeons, one surgical fellow, two surgical residents, and two interns serve the transplant recipients. Three internists, one pediatrician, and one or two fellows serve the patients on dialysis. The primary purpose of the dialysis unit is to care for acute renal failure and serve the transplant unit. No long-term hemodialysis patients are maintained on the unit except for very small children because facilities for their care elsewhere are lacking. Three dialysis units, St. Paul Ramsey Hospital in St. Paul, Methodist Hospital in St. Louis Park, and Miller Dwan Hospital in Duluth, cooperate with the transplant unit at the University Hospital. They accept patients independently of the Minneapolis center but all transplantations on these patients are performed at the University Hospital.

Three other completely independent transplantation-dialysis centers exist in Minnesota: the Veteran's Administration Hospital and Hennepin County General Hospital in Minneapolis, and the Mayo Clinic in Rochester. All these units also cooperate with the University Hospital by maintaining some patients on chronic hemodialysis while they await cadaver donor organ transplantation at the University Hospital.

Cadaver Retrieval

A special donor organization is maintained at the University Hospital. It is headed by a "donor doctor" who is available for consultation regarding potential donors. An airplane containing a portable kidney preservation unit[1] is stationed at the University and makes flights to outlying hospitals to obtain cadaver kidneys. Twenty to fifty percent of these kidneys are supplied to the other transplantation units in Minnesota or flown out of state.

Selection of Patients

Our criteria for the acceptance of a prospective transplant recipient are extremely liberal. Patients from the newborn period to the age of 72 years have been transplanted and diabetic patients are regularly accepted. Absence of a normal urinary bladder has not been regarded as an absolute contraindication to transplantation and patients have been transplanted into ileal loops. Less than four percent of all patients evaluated by us for transplantation have been rejected. Almost all of those rejected for transplantation are offered chronic hemodialysis. The reasons for rejection for transplantation have been extreme age, wide spread incurable malignancies, or severe and multiple complications of diabetes in addition to renal failure.

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The main indication for starting hemodialysis in preparation for transplantation is a plasma creatinine in the range of 12-15 mg percent. The patient should be started on dialysis even earlier if symptoms of severe hypertension, anemia requiring repeated transfusions, severe bone disease, polyneuropathy or, if he is in the pediatric age group, failure to grow, are present. Diabetic patients should probably be started even earlier because there is evidence[2] that the combination of hypertension and uremia leads to marked aggravation of diabetic retinopathy. It may be that early transplantation (when the creatinine is five-seven mg percent) can prevent or delay the tragic complication of blindness.

Treatment

The prospective transplant recipient in end-stage renal failure undergoes a series of routine procedures (Figure 1).

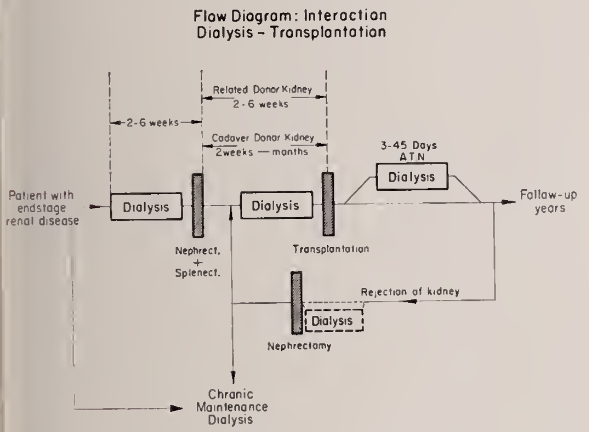

Fig. 1—Flow diagram of the interaction between dialysis and transplantation in the management of a patient with end-stage renal failure.

After an initial stabilization period on dialysis, the patient undergoes bilateral nephrectomy and splenectomy. Patients with related donors usually receive their transplant within one to two weeks, while those awaiting cadaver transplants are usually transferred to other hemodialysis units from which they are recalled when a cadaver kidney becomes available. Tissue typing and cross matching have been performed regularly since 1969, but the patient's physical condition, rather than tissue typing, determines which patient receives a cadaver kidney. Some kidneys do not function immediately after grafting, and these recipients must receive dialysis for acute renal failure before their kidney returns to normal function. Some patients eventually reject their kidneys, and they are returned to dialysis either to await retransplantation or to continue on chronic hemodialysis elsewhere. Antilymphocyte globulin is given to all patients. Routine immunosuppression including azathioprine and prednisone is then rapidly tapered. Acute rejection episodes are treated with methylprednisolone intravenously, an increase in oral prednisone, and local radiation of the graft.

Results

Three hundred seventy-four patients received 424 renal transplants between 1968-1973 at the University Hospitals. As of April 1, 1974, 295 patients (79 percent) are still alive, and 283 (67 percent) of the original 424 kidney grafts are functioning. Only 12 patients have been returned to hemodialysis to await retransplantation.

Non-Diabetic Patients

Patient Survival: Recipients who do not have diabetes mellitus account for 315 of the total patients; 252 (81 percent) are still alive. Except for 11 patients who are on dialysis awaiting retransplantation, all the other survivors have functioning kidneys, and 90 percent of them have creatinine levels below 1.9 mg per 100 ml (Table 1). It is evident that the prospect for survival after a related kidney graft is better than after a cadaver kidney transplant. Figure 2 shows the cumulative survival calculated according to the method of Merrell and Shulman.[3] The six year survival, independent of age, group is approximately 90 percent following a related kidney graft. Figure 3 clearly illustrates that the results are less good in the patients who receive cadaver kidneys. In this group increasing age is associated with decreasing survival. The cumulative survival is 70 to 80 percent for a three to five year period for the two categories of ages, six to 14, and 15 to 45 years. The survival is only 40 percent for the patient above age 45. None of

TABLE 1
Surviving Nondiabetic Patients

Recipient Age	1st Kidney Cadaver	1st Kidney Related
0-5	0/4 (0%)	11/12 (92%)
6-14	8/9 (89%)	29/34 (85%)
15-45	55/71 (77%)	84/94 (90%)
>45	25/46 (54%)	40/45 (89%)
Total	88/130 (68%)	164/185 (89%)

the four patients who were below the age of five, and received cadaver kidneys, survived. Three of these children were newborn babies, the fourth was transplanted after bilateral nephrectomy for Wilms' tumor.

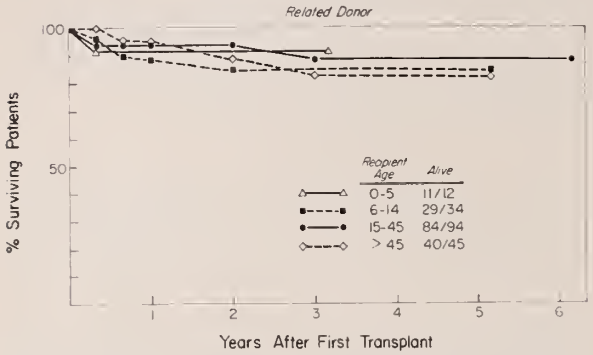

Fig. 2—Cumulative survival of non-diabetic patients after transplantation from a related donor. The survival of all age categories is between 80 and 90 percent, three to six year survival.

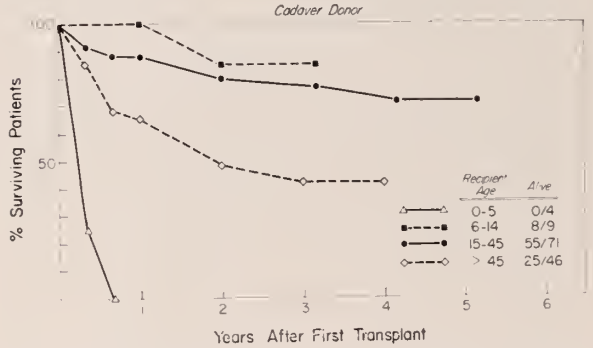

Fig. 3—Cumulative survival of non-diabetic patients transplanted with cadaver kidneys. Approximately 80 percent survival is achieved in the patient age six to 45. A 45 percent four year survival is observed in the older patient and no patient below age five survived if he first received a cadaver kidney.

Table 2 outlines survival in our patients after a second kidney transplant. If the first kidney is from a related donor there is no difference in survival between a recipient of two kidneys and the recipient of only one. However, two consecutive cadaver kidneys carry a lower survival, 50 percent. Three of our patients received three kidneys. In all instances the first kidney was from a related donor and the following two kidneys were from cadaver donors. Two of these patients are alive four and three years after the first transplant, the other patient died one half year after the first transplant. One child, a 12-year-old girl, is alive after a fourth transplant performed two years ago, three and one half years after her first transplant. Retransplantation is a successful and valid procedure in the non-diabetic patient.

TABLE 2
Nondiabetic Patient Survival after Retransplantation

1st Kidney	2nd Kidney	Survival
Related	Related	9/10 (90%)
Related	Cadaver	11/12 (92%)
Cadaver	Related	—/— —
Cadaver	Cadaver	7/14 (50%)

Kidney Survival

Table 3 outlines the total functioning kidneys in our series. Two thirds (241 of 360) of all the kidneys we transplanted into non-diabetic patients survived. There is a better functional survival of related kidneys than of cadaver kidneys, 76 percent versus 56 percent.

TABLE 3
Total Functioning Kidneys

Recipient Age	Cadaver Kidneys		Related Kidneys	
0-5	1/6	(16%)	10/13	(77%)
6-14	10/17	(59%)	26/39	(67%)
15-45	54/86	(63%)	76/99	(77%)
>45	27/55	(49%)	37/45	(82%)
Total	92/164	(56%)	149/196	(76%)

The cumulated functional survival of the related and cadaver donor kidneys transplanted in non-diabetics is shown in Figures 4 and 5. For related kidneys (Figure 4) there is no great difference between the various age categories. However, of the cadaver kidneys (Figure 5) transplanted into patients older than 45 years, only approximately 40 percent show a functional three to four year survival as compared to 60 percent three to five year survival in the age group of six

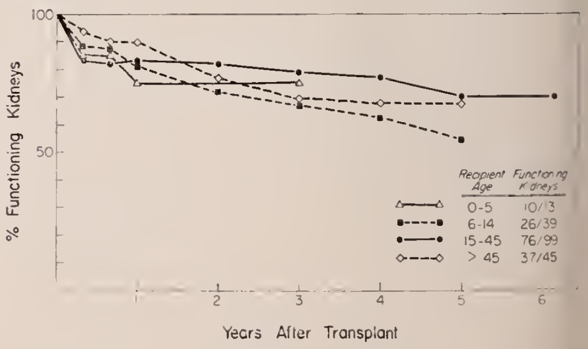

Fig. 4—Cumulative functional survival of all related kidneys. In all groups a 70 percent, three to six year survival is encountered.

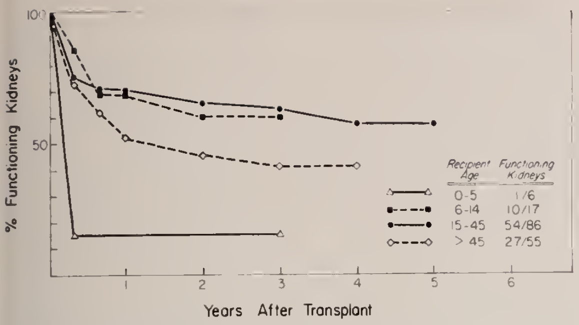

Fig. 5—Cumulative functional survival of all cadaver kidneys. A 60 percent, three to five year survival of these kidneys is achieved if the recipient was age six to 45 years. It is only 40 percent in a patient above age 45 and only a single kidney survived in a patient younger than age five.

to 45 years. Only one cadaver kidney transplanted into a patient younger than the age of six survived. This kidney was transplanted into a four-year-old boy who had rejected a grandmother's kidney after two months. The cadaver kidney still has excellent function three years after transplantation.

Diabetic Patients

Forty-three of the 59 (72 percent) patients with diabetes who received a kidney transplant are alive. Nine of 15 (60 percent) of these patients survive after cadaver transplantation versus 34 of 44 (77 percent) patients who received a related first transplant. One half of the cadaver kidneys (nine of 18) have functional survival versus 33 of 46 (72 percent) related kidneys. One patient has been returned to dialysis after failure of first a related, then a cadaver kidney. One patient has a functioning second related graft, but three patients died after retransplantation. Clearly, retransplantation is not as successful in the diabetic patient as it is in non-diabetic patients. It is obvious that both the cadaver and the related donor results are less good than in the non-diabetic group. There is also a basic difference in mortality of the diabetic patients after transplantation. While most of the losses in non-diabetic patients occur during the first or second year, there is continual loss of diabetic patients due to late cardiovascular complications.

Growth

Of the 59 children below age 14, who could be observed for more than one half year after transplantation, approximately 40 percent showed a growth spurt or grew normally within ± 1 SD of the normal growth curve. Half of the patients grew normally but below 1 standard deviation and approximately 10 percent showed no growth whatever after transplantation.

Recurrence of Original Kidney Disease

It is frequently difficult to differentiate between recurrence of the original kidney disease and a rejection episode. Approximately one half of the patients with steroid resistant nephrotic syndrome have had recurrence of nephrosis in their transplanted kidney.[4] In contrast, no patients with congenital nephrotic syndrome have shown recurrence.[5] One half of the patients with membrano proliferative glomulonephritis seem to have a slow recurrence of the diseases in their kidneys. Lupus nephritis, however, does not seem to recur. Two patients with Goodpasture's syndrome have also developed deposition of antibody to glomular basement membrane in their transplant but two patients with cystinosis have had no recurrences. Clinical diabetic kidney disease has not yet recurred in any transplanted kidney but the longest follow-up period is only four years.[2]

Early Complications of Transplantation

Early complications following kidney transplantation are either urological or vascular, and occur in three percent of the recipients. Hyperacute rejection with loss of the kidney has occurred in approximately three percent of our patients. Acute tubular necrosis occurred in ten percent of the kidneys from related donors and 25 to 30 percent of the recipients of cadaver kidneys. This complication has no adverse effect on either the survival of the patient or on the ultimate function of the kidney.[6] The early occurrence of bacterial complications to transplantation is no longer a major problem, however, infections with viruses of the herpes group with high spiking fever with or without functional deterioration of the kidney graft is one of the major early clinical complications.

Late Complications of Transplantation

The late complications of transplantation are essentially those of steroid therapy. Cushingoid appearance, particularly disturbing to some young women, occurs temporarily in about 20-30 percent of the patients. Steroid diabetes has occurred in one fifth of the patients above age 45, more commonly in women, and has been easily managed.[7] Hypertension occurring in approximately 10 to 30 percent of the patients normally responds to minimal antihypertensive therapy. Bone complications including aseptic necrosis of the femoral head, calcaneus and tibial condyles, have occurred in four to six percent of the patients, particularly in the children. Cataracts, of a posterior lenticular type, occur but usually do not interfere with vision and have not required operation in our patients. Only one death from malignancy has occurred in our patients. All patients are continued on immunosuppressive therapy for the rest of their lives and they are therefore at risk to develop infectious complications. These infections are frequently caused by unusual organisms as fungi, tubercle bacilli, or viruses. The clinical course is also bizarre. Consequently, any localized swelling or temperature elevation is a warning signal in these patients requiring exhaustive and unusual diagnostic procedures.

Discussion

Renal transplantation is an established procedure for the treatment of end-stage renal failure with a 90 percent six-year survival after related donor transplantation. The success rate has greatly improved; cadaver transplantation is now three times as successful as it was during the first five years after transplantation, at the University of Minnesota.[8] Related transplantation has improved approximately 50 percent, from 60 to 90 percent six year survival.[18] The results at the University of Minnesota are considerably better than those reported by large transplant registries.[9,10] In part this may be due to the fact that we perform over 100 transplants each year. Centers that perform more than 25 transplants per year have higher survival rates than those who do fewer transplants.[9] Another reason for our success rate may be the use of antilymphocyte globulin.[12,13]

Transplantation from a related donor is the treatment of choice for end-stage renal failure and is clearly superior to cadaver donor kidney transplantation or chronic hemodialysis in any age group. In our opinion, cadaver transplantation in the age group six to 45 is also superior to that of chronic hemodialysis. However, in the patient over age 45 who do not have related donors, transplantation may not be superior to chronic hemodialysis. Lewis and co-workers[14] have reported a survival rate in patients above 45 on chronic hemodialysis approximately equal to that experienced by our older patients receiving cadaver transplantation. Cohen and co-workers[16] have reported a higher success rate in the dialyzed patients over age 49 while Pendras and co-workers[15] have reported a lower survival rate, 40 percent at the end of two years, for dialyzed patients above age 56. Overall the success rate is not as high for the older patients with end-stage renal failure and clear guidelines for the treatment of these patients are yet lacking. One possible solution may be a careful investigation of the patient and the knowledge of the prevalent causes of death in chronic hemodialysis and transplantation. Fifty percent of all deaths in transplantation are directly or indirectly caused by infections.[9,17] Fifty percent of the deaths in chronic hemodialysis are caused by cardiovascular accidents.[10] Cardiovascular premature aging may be an important survival limiting factor in the chronic hemodialysis program.[18] Thus, an older patient who already has cardiovascular problems may benefit more from transplantation than from chronic hemodialysis and a paitent who is susceptible to infections, particularly one with pre-existing lung disease or who is a heavy smoker, may be better off on chronic hemodialysis.

The success rate of transplantation in the diabetic patient is much less than that in the non-diabetic. Particularly discouraging has been the observation that the death in diabetics after transplantation continues at a steady rate rather than leveling after one or two years as it does for the non-diabetic patients (Figure 2). However, the success of chronic hemodialysis for the diabetic patient, as so far reported, has been much less than the success of transplantation,[19-21] and only Shapiro and co-workers[22] have reported patients with diabetes who have survived even 2½ years on chronic hemodialysis.

Transplantation has been recognized by the United States Congress and after the implementation of Public Law 92-603, July 1973, all patients with end-stage renal failure will have their care, including renal transplantation, paid for by the Federal Government. The main problem in transplantation relates to rejection and complications of immunosuppressive therapy. More specific manipulations of the immune response perhaps through the development of clinical methods for the use of enhancement or the induction of tolerance will hopefully improve this situation.[23]

Acknowledgment

In spite of the fact that Minnesota is a relatively small state, the University of Minnesota transplantation program is presently the largest in the world. It is truly a cooperative effort. Without the help of hospitals throughout Minnesota and in neighboring states in supplying us with cadaver organs, this would not be possible. With approximately 150 to 200 patients per one million inhabitants in Minnesota having been cared for either by transplantation or chronic hemodialysis, Minnesota is doing twice as well as the next best reported area, Denmark which has 88 patients per one million inhabitants cared for by either treatment.[10] We thus feel it is appropriate to end this paper by thanking our colleagues, physicians, nurses, administrators, and other personnel in hospitals throughout Minnesota and the neighboring states for their help in securing cadaver organs for us.

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In a country in which, to play a social part, you must either earn your income or make believe that you earn it, the healing art has appeared in a high degree to combine two recognized sources of credit. It belongs to the realm of the practical, which in the United States is a great recommendation; and it is touched by the light of science—a merit appreciated in a community in which the love of knowledge has not always been accompanied by leisure and opportunity. It was an element in Doctor Sloper's reputation that his learning and his skill were very evenly balanced; he was what you might call a scholarly doctor, and yet there was nothing abstract in his remedies—he always ordered you to take something.*

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*Henry James: Washington Square, Chapter I. 1880.

Diagnostic and Operative Hysteroscopy[*]

RAFAEL F. VALLE, M.D. and JOHN J. SCIARRA, M.D., Ph.D.

The history and technique of hysteroscopy (gynecologic endoscopy) are reviewed, and indications and contraindications for its use are summarized. Use of the technique is reported in a series of 75 patients from the Hennepin County General Hospital (HCGH) and the University of Minnesota Hospitals (UMH). Hysteroscopy is a safe, acceptable, promising, and versatile mode of diagnosis and treatment.

THE INTRODUCTION OF fiberoptics in medicine was an important step in the development of new endoscopic techniques. Gynecologic endoscopy is a well established clinical diagnostic tool, with intraperitoneal visualization possible by both culdoscopy and laparoscopy. Hysteroscopy makes possible visualization of the cervical canal and uterine cavity by means of an instrument which includes a metallic sheath and a telescope receiving light from a fiberoptic light source. A solution or a gas is used to distend the uterine cavity.

Although over a century old, hysteroscopy has only recently been widely investigated. Previous investigators had difficulty maintaining uterine distention, and bleeding produced by the instrument made good visualization difficult. However, since the work of Edström and Fernström from Sweden in 1970, using 35% dextran as a medium to distend the uterus, the potential of the improved technique has proved to be broad and promising.[1] Lindemann has pioneered the use of CO_2 as a medium for distending the uterine cavity.[2]

Development of Hysteroscopy

Pantaleoni was the first to perform hysteroscopy in a living human being in 1869, when he used his "endoscope" for visualization of the uterine cavity and removed a polypous growth in a 60-year-old woman affected with postmenopausal bleeding.[3] The technique was then forgotten. In 1925, interest was renewed by several investigators, especially Rubin, in the use of CO_2 for distention of the uterine cavity. Von Mickulicz-Radecki and Freund, in 1927, introduced the idea of electrocoagulation of the intramural portion of the tubes. Norment, in this country, worked for over 30 years with several models of hysteroscopes, including a water-rinsing system and a hysteroscope with a rubber balloon attached to its distal part and insufflated with air. Results with the above instruments and techniques were never satisfactory.

In 1962, Torsten Silander introduced a hysteroscope with a latex rubber balloon attached to the distal portion for distention of the uterine cavity by means of normal saline instead of air. This provided acceptable visualization, but the uterine cavity remained inaccessible for biopsies or other types of surgical intervention.[4]

In 1970, Edström and Fernström published results with the use of 35% dextran (molecular weight of 70,000) for distention of the uterine cavity.[1][†] This allowed, indeed for the first time, not only excellent visualization, but also biopsies and other surgical manipulations within the uterine cavity.[5] Presented here is a history of the development of this technique.

History of Hysteroscopy

Investigator	Year
Pantaleoni	1869
David	1908
Heineberg	1914
Rubin	1925
Seymour	1926
Von Mickulicz-Radecki-Freund	1927
Gauss	1928
Shroeder	1934
Shack	1936
Segond	1934-37
Norment	1942-70
Englund-Ingelman-Sundberg-Westin	1957
T. Silander	1962
Edström-Fernström	1970

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[*] This paper was presented in part at the Minnesota State Obstetrical and Gynecological Society, December 1, 1973.

Donald W. Freeman, M.D. provided valuable comments and suggestions in the preparation of this paper.

[†] The Hyskon® (hysteroscopy solution)—30% w/v dextran 70 in dextrose—used in this study was supplied by Pharmacia Laboratories, Inc., Piscataway, New Jersey, 08854.

Since 1970 several media for distention of the uterine cavity have been used successfully; 5% dextrose, CO_2 and normal saline.[2,6]

Materials and Methods

We began to perform hysteroscopy at the University of Minnesota Hospitals and Hennepin County General Hospital (HCGH) in the winter of 1972, although few examinations were done initially because of technical difficulties in obtaining instruments and ancillary equipment. A proper setting for hysteroscopy was established in mid-1973.

At the University of Minnesota Hospitals, patients were from the Infertility Clinic, and hysteroscopy was added in selected patients as a complementary diagnostic method to evaluation of female infertility. The patients examined at Hennepin County General Hospital were chosen from the out-patient gynecology clinic. The instruments used are hysteroscopes manufactured by Storz and American Cystoscope Makers, Inc. (ACMI). Both hysteroscopes are rigid; they differ essentially in that the ACMI has a more oval sheath than the Storz, which is circular (Figure 1).

The distending media have varied in both institutions. Dextran 35% has been used at the University of Minnesota Hospitals, where hysteroscopy has usually been performed under general anesthesia, because of concomitant laparoscopy or dilatation and curettage (D & C).

Dextran 35%, with a molecular weight of 70,000 and a viscosity of 225 centipoise at 37° C, has the desirable properties of being viscid, optically clear, and not readily miscible with blood. It also offers a high refractory index, and because its flow around the sheath is minimal, a smaller quantity is needed during the procedure. However, it is not commercially available in the United States at the time of writing.

At Hennepin County General Hospital, most of the procedures have been performed under a paracervical block in the gynecology out-patient clinic, and only those patients scheduled for additional surgical intervention have received general anesthesia. In most hysteroscopies at HCGH dextrose 5% has been employed for uterine distention.

Dextrose 5%, when used for distending the uterine cavity, must be administered under specific pressure for each individual patient. It does not mix with blood, produces little or no bleeding, and is readily available at a low cost.[7]

Technique

The simple technique of hysteroscopy can be summarized as follows (Figure 2).

1. Once the patient has been selected for hysteroscopy, a pap smear and cervical-vaginal smear and cultures are done, the latter to rule out active infection.
2. After explanation of the procedure, the patient is told to void before being placed on the examining table.
3. The patient is placed in the dorsal lithotomy position and vulva and vagina are cleaned with an antiseptic solution.
4. The cervix is visualized and a paracervical block performed with carbocaine 1%, 10 cc in each side. Ten minutes are allowed for the anesthetic to take effect. General anesthesia may also be employed.
5. The uterine cavity is sounded and the cervical canal dilated to #7 or #8 Hegar, depending upon the instrument used.
6. The hysteroscope, already attached to a light source and a solution of dextrose 5% or other appropriate fluid, is introduced. Inflow pressures vary with individual patients.
7. Three to five minutes is sufficient for good visualization of the uterine cavity, including the tubal ostia.
8. Any unusual tissue, polyps or submucous myomas are biopsied or removed with special biopsy forceps.
9. When hysteroscopy is performed under general anesthesia, it is usually followed by additional surgical procedures. On many occasions, a concomitant laparoscopy or D & C is performed, especially in cases of suspected

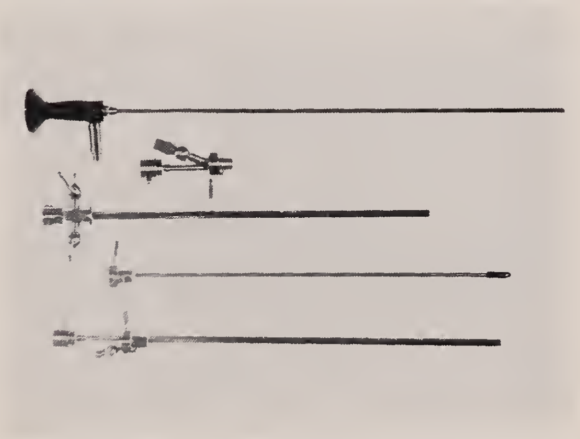

Fig. 1—Disassembled hysteroscope (Storz). Top to bottom: foroblique telescope; separable bridge with operating channel; outer sheath; obturator; nonseparable bridge.

peri-tubal adhesions or in the presence of intrauterine synechiae.[8] We prefer general anesthesia only when additional surgical intervention is required; otherwise paracervical block suffices.

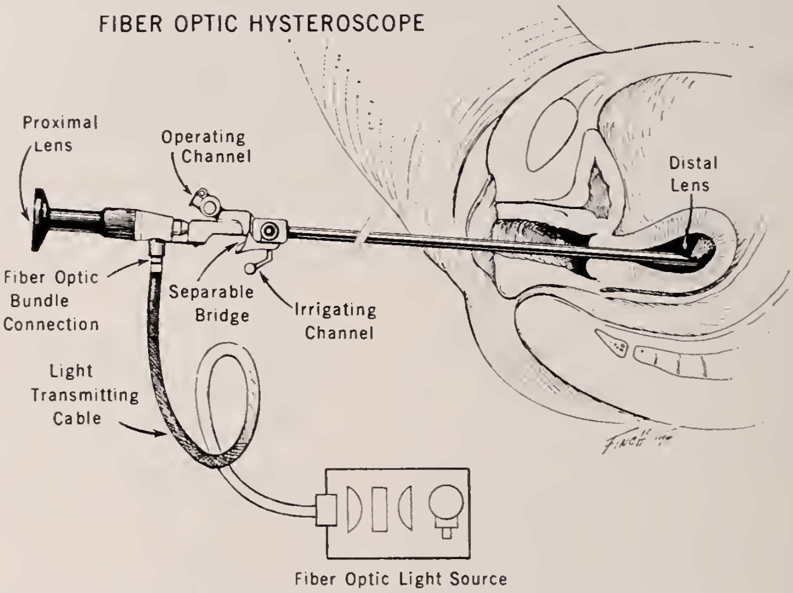
FIBER OPTIC HYSTEROSCOPE
Proximal Lens
Operating Channel
Distal Lens
Fiber Optic Bundle Connection
Separable Bridge
Irrigating Channel
Light Transmitting Cable
Fiber Optic Light Source

Fig. 2—Diagrammatic representation of the hysteroscope in use.

Indications for Hysteroscopy

The indications for hysteroscopy are multiple. As the technique improves, more applications are surely to be found and the potential of the procedure will be broadened (Figure 3).

The most common uses may be listed as follows:

1. Dysfunctional bleeding.
2. Suspected submucous myomas or polyps.
3. Non-visualization of IUD filaments at the cervix. Suspected foreign bodies within the uterine cavity.
4. Postmenopausal bleeding.
5. Infertility, primary and secondary, especially if any anomalies or defects are seen by hysterosalpingography.
6. Intrauterine adhesions.
7. Patients with habitual abortion, for exploration of the cervical canal and uterine cavity.
8. For sterilization by intrauterine electrocoagulation of the intramural portion of the fallopian tubes.[6]

Other situations in which hysteroscopy is presently being evaluated include:

1. Study of physiologic cyclic changes of the endometrium, proliferative and secretory phase.
2. Tubal catheterization for recording of tubal motility and biochemical study of the tubal milieu.[9]
3. Splinting of proximal stumps prior to tubal plastic surgery.
4. Possible reversible occlusion of the tubes by means of substances inserted in the uterotubal ostia.

Contraindications to Hysteroscopy

There are three major contraindications: acute pelvic inflammatory disease, pregnancy, and profuse bleeding. Previous infection must be ruled out before hysteroscopy is undertaken. The technique may be modified and used as amnioscopy in pregnancy. This may be of value in diagnosis of premature rupture of the membranes

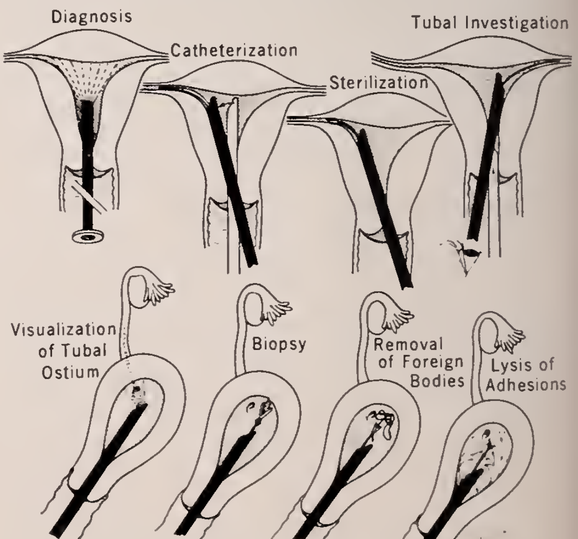
Diagnosis
Catheterization
Sterilization
Tubal Investigation
Visualization of Tubal Ostium
Biopsy
Removal of Foreign Bodies
Lysis of Adhesions

Fig. 3—Uses of hysteroscopy.

and in the detection of chronic fetal distress by color changes in the amniotic fluid.[10]

Possible Complications

The use of any surgical instrumentation within the uterine cavity requires experience and delicacy, and unnecessary manipulation must be avoided to prevent damage to the endometrial lining. Careful selection of patients and adherence to the protocol will prevent exacerbation of an already present infection or the introduction of new bacteria. Significant complications which have been reported include bleeding, uterine perforation and infection. Uterine perforation, however, has been reported to occur at uterine sounding or cervical dilatation, and these cases have been relatively few.

Advantages

Hysteroscopy offers several advantages over other methods of diagnosis and surgical therapy of pathologic lesions within the uterine cavity. The most relevant are:

1. Direct visualization of the endometrial cavity, obviating diagnostic errors associated with D & C and endometrial biopsies:
2. Its applicability as an out-patient procedure requiring only local anesthesia;
3. Its acceptability to patients;
4. Its minor risks;
5. Its brevity (average total duration of the procedure is usually about 5 minutes).

This endoscopic technique obviously has its limitations. It cannot be considered as replacement for other diagnostic methods, but rather as adjuvant and complement, to refine diagnostic accuracy and provide better therapy.

Preliminary Results

From September, 1973, to March, 1974, we performed hysteroscopy in 75 patients. In the group of patients at the University of Minnesota Hospitals, ages ranged from 22 to 39 years; in the patients at Hennepin County General Hospital, ages ranged from 20 to 68 years. Hysteroscopic findings were abnormal in 52 (69%); 23 patients (31%) showed normal findings.

Hysteroscopic examination was done under paracervical block in an outpatient clinic visit in 41 patients and under general anesthesia in 34, because of concomitant or subsequent surgical intervention, such as hysterectomy, laparoscopy, or D & C (Tables 1 and 2).

TABLE 1
Preoperative Diagnoses

Metrorrhagia	22
Dysfunctional Bleeding	9
Myomatous Uterus	1
Postmenopausal Bleeding	19
Foreign Body	8
Primary Infertility	6
Secondary Infertility	2
Habitual Abortion	3
Suspected Uterine Anomaly	1
Suspected Uterine Perforation	2
Defect on Hysterosalpingography	2
Total	75

TABLE 2
Hysteroscopic Findings

Normal	23
Septate Uterus	3
Submucous Myoma	5
Endometrial Polyps	23
Scar Defect	1
Foreign Body (6 IUD's-1 Laminaria)	7
Atrophic Endometrium	6
Adenocarcinoma of Endometrium	1
Intrauterine Adhesions	4
Uterine Perforation	2
Total	75

All patients tolerated the procedure well, under both types of anesthesia. In several instances, hysteroscopy enabled the investigators to make precise diagnoses of developmental abnormalities, myomas, and other pathological conditions which the usual diagnostic methods did not.

Complications

In our series, two uterine perforations occurred at the time of uterine sounding, while the procedure was being performed under general anesthesia. The defect was observed in subsequent hysteroscopy with concomitant laparoscopy, and there were no untoward effects.

Comment

With the new engineering achievements in instrumentation, as well as the introduction of cold light transmitted by fiberoptics, the hysteroscope has been technically refined. Accordingly, the technique has been revived and is being evaluated with great interest.

Direct visualization of the uterine cavity and endometrial lining enables the endoscopist to explore this previously inaccessible area and, by direct observation, to take selective biopsies and perform intrauterine surgical intervention. The gynecologist no longer must rely solely on blind curettage or abnormal hysterographic shadows; a much more accurate technique is available.[11]

Learning hysteroscopy may be difficult; many abnormalities are not readily recognizable to the viewer and require experience for proper interpretation. Intrauterine manipulation and instrumentation, such as performance of targeted biopsies and avoidance of unnecessary trauma to the rest of the endometrium, require experience, as well. Experience, however, is readily available, and the endoscopist soon acquires familiarity with direct observation of the intrauterine cavity. Surgical intervention within the uterine cavity should be delayed until experience with intrauterine visualization and observation, especially at the uterotubal junction, has been acquired.

Development of modern hysteroscopy revived interest in utero-tubal occlusion by offering direct visualization of the tubal orifices. This makes possible the introduction of specially designed electrodes into the intramural portion of the fallopian tubes and the delivery of a specific current to destroy the lining of the lumen and the surrounding muscular layer, resulting in its complete occlusion. A program of hysteroscopic sterilization has been initiated by the authors; and the results of this clinical investigation will be the subject of a subsequent report.

In all of our patients who underwent other procedures, such as hysterectomy or D & C, our hysteroscopic diagnosis was confirmed.

We find hysteroscopy to be valuable, safe, well accepted by patients, and promising because of its simplicity. It can be performed on an outpatient basis, sparing general anesthesia and expensive, time-consuming hospitalization.

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It's The Law

$40,000 for Nurses' Negligence Resulting in Amputation

A 79-year-old patient was admitted to the hospital because of pneumonia. On the second day of his stay the nursing staff were unable to obtain a blood pressure reading in the patient's right arm. The patient complained of coldness and numbness in his right hand. This information was not transferred to the admitting physician and was not entered in the nurses notes until two days later.

On the third day of his hospital stay, the patient did not complain of pain in his arm to his admitting physician and the physician did not examine the arm. Later that same day, a registered nurse phoned the physician to report the patient's complaint of pain in the right arm. The physician prescribed Tylenol and Codeine.

On the fourth hospital day the hand was cyanotic and mottled. The physician examined the hand, called a vascular surgeon, however, the circulation of the hand was severely compromised and the entire hand was finally amputated.

The patient sued the hospital and treating physician but at trial the complaints against the physician were dismissed and the verdict was awarded against the hospital and the hospital was assessed $40,000 damages.

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Minneapolis, Minnesota

Walton v. Providence Hospital (Cal. Super Ct., Alameda Co., Docket No. 433105, March 18, 1974. The Citation 29:7, July 15, 1974.

Hearing Loss and Thyroid Disorders

WILLIAM L. MEYERHOFF, M.D.*

The incidence of hearing loss in thyroid abnormalities is frequent enough to warrant study by the practicing physician. The otolaryngologist should be aware of the association, manifestations and therapy.

HEARING LOSS, BOTH congenital and acquired, can be associated in a more than coincidental manner with disorders of almost every organ system, the thyroid gland being no exception. The first description of the joint occurrence of thyroid abnormalities and hearing loss dates back to the early 13th century when Jacques de Vitry, an itinerant preacher, described many deaf-mutes among the goitrous dwarfs of the St. Bernard Pass in Switzerland.[1] Although the subsequent literature is replete with speculations and observations, complete understanding of the thyroid gland-auditory system relationship is lacking. Several known syndromes, seemingly unrelated except for their association of hearing loss and thyroid abnormalities, have been described and, from the standpoint of hearing loss, may be conveniently divided into four categories: (1) Non-genetic congenital; (2) Non-genetic acquired; (3) Genetic congenital; and (4) Genetic delayed (Table).

Classification

Non-genetic Congenital

This category includes endemic cretinism. The first description of cretinism (a contraction of Christian, one of God's creatures) was recorded in the Encyclopedie ou Dictionnaire Raisonne des Sciences in 1754, ". . . they are deaf, dumb, imbecile, almost insensitive to blows, and carry goiters hanging down to the waist; rather good people otherwise, they are incapable of ideas, and have only a sort of violent attraction for their wants. They abandon themselves to the pleasures of the senses of all kinds, and their imbecility prevents them from seeing any crime in this."[2] It has been estimated that up to 70% of cretins suffer from hearing loss. The hearing loss has been attributed, by various authors, to both slow mentation and anatomic abnormalities of the cerebral cortex, middle ear and petrous portion of the temporal bone. Thyroid therapy, if initiated early, is of some systemic benefit, but generally is of little value in restoration of hearing.[3-6]

Non-genetic Acquired

This category includes sporadic (non-endemic) athyrotic cretinism and juvenile and adult hypothyroidism. Up to 25% of patients with acquired hypothyroidism suffer from hearing loss which improves with thyroid therapy. The hearing loss may be moderate to severe and is usually sensorineural, although there may be a conductive component. The hearing loss is often associated with other otologic symptoms such as tinnitus, vertigo and ataxia. The degree of the hearing loss is independent of the degree of the hypothyroid state.[7] Many anatomic abnormalities of the auditory system have been described which could, in part, account for this hearing loss. Included are endolymphatic hypertension, loss of hair cells, thickening of the tympanic membrane, thick-

TABLE

- **I. Non-Genetic Congenital: Endemic Cretinism**
- **II. Non-Genetic Acquired**
  - **A. Sporadic (Non-Endemic) Athyrotic Cretinism**
  - **B. Juvenile Hypothyroidism**
  - **C. Adult Hypothyroidism**
- **III. Genetic Congenital: Sporadic (Non-Endemic) Goiter and Hearing Loss (Pendred's Syndrome)**
- **IV. Genetic (Acquired) Delayed: Sporadic (Non-Endemic) Goitrous Cretinism. (Inborn Errors of Thyroid Metabolism)**

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*Medical Fellow, University of Minnesota Medical School, Minneapolis.

This study is supported by a Deafness Research Foundation grant.

ening of the middle ear mucosa, eustachian tube obstruction, alteration of the middle ear ossicles, changes in the spiral ganglion, absence of cochlear potential, degeneration of the tectorial membrane and degeneration of the organ of Corti in general.[8,9] These observations have gone a long way to aid the understanding of hypothyroid deafness, but the exact mechanism remains unknown. The non-endemic athyrotic cretins lack the severe morphologic changes of the endemic cretins because their mothers are euthyroid and therefore their intrauterine development is normal. The etiology and pathophysiology of their hearing loss is the same as that described for juvenile and adult hypothyroidism. As mentioned above, thyroid therapy may reverse the hearing loss in this category.

Genetic Congenital

This category includes sporadic (non-endemic) goiter and hearing loss (Pendred's Syndrome). In 1896 Vaughn Pendred, an English country general practitioner, was the first to describe congenital deafness and sporadic goiter. Pendred's Syndrome is genetically determined by an autosomal recessive gene. The hearing loss is present at birth, moderate to severe in degree, sensorineural in nature and worse in the high frequencies. Although these patients develop a goiter in their early teens they are usually euthyroid and thyroid hormone does not improve the hearing. The thyroid defect is thought to be a peroxidase deficiency which blocks the organification of iodine and is felt to be an independent expression of the same gene which is responsible for the hearing loss. The pathophysiology of the auditory defect is not entirely understood although temporal bone histopathology has revealed a Mondini-like defect in several cases. Genetic counseling is advised.[1,10,11]

Genetic Delayed

This category includes sporadic (non-endemic) goitrous cretinism. These patients are hypothyroid due to a genetic error in metabolism of thyroid hormone. The genetic trait appears to be simple recessive. The hearing loss, usually mixed, is probably the result of congenital hypothyroidism and therefore the clinical findings are similar to those found in non-genetic acquired hypothyroidism. As in sporadic athyrotic cretinism, the mothers of the sporadic (non-endemic) goitrous cretins are usually euthyroid, sparing these patients the severe morphologic abnormalities of the endemic cretins. Histologic studies of the inner ear are not available to date. Since the hearing loss is apparently related to the hypothyroid state and not a genetic expression as in Pendred's Syndrome, thyroid hormone may prevent or reverse the hearing loss. Understanding of the genetic transmission may help avoid the unfortunate effects of juvenile hypothyroidism.[12]

Discussion

The manifestations of hypothyroidism are many and well-known to the clinician. In addition to hearing loss they include obesity, constipation, hoarseness, hair loss, dry skin and sluggish mentation. Cretinism is simply congenital hypothyroidism and, in addition to hearing loss, if untreated, will manifest a multitude of similar findings including constipation, thick tongue, dry skin, hair loss, retardation of osseous development, delayed dentition and mental retardation. Abnormalities are most severe in endemic cretins due to the insufficient level of circulating thyroid hormone during intrauterine development. If treatment with thyroid hormone is begun early, most manifestations of hypothyroidism are reversible.

Pendred's Syndrome, on the other hand, is a genetically determined sensorineural hearing loss with goiter. Development is otherwise normal in all respects. The diagnosis is made by a positive thiocyanate flush in association with the above two clinical manifestations. Treatment is aimed at the cosmetic and physiologic complications of the goiter, as the hearing loss is irreversible. As mentioned earlier, genetic counseling in Pendred's Syndrome and sporadic (non-endemic) goitrous cretinism serves a definite value.

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8-12. Will be found on page 916.

Methadone Maintenance Treatment

A Report On Over Three Years Experience[*]

V. B. TUASON, M.D., F.R.C.P.(C)[†] and REV. WALTER L. JONES[‡]

The 41 months' experience of a methadone treatment center is reported.

METHADONE MAINTENANCE has gained broader acceptance in the treatment of narcotic addiction, despite continuing medical, legal, and moral disputes over its use. The Federal Register of December 15, 1972 set forth regulations to provide for a closed system of methadone distribution only through approved programs. This report describes the experience of such an approved program with particular reference to patient performance.

St. Paul Drug Rehabilitation Center, Inc. is a community based methadone treatment program serving the drug (heroin or other morphine—like drugs) dependent person according to guidelines of the Department of Health, Education and Welfare—Food and Drug Administration. The Center is a non-profit corporation directed by an executive administrator who is responsible to a board consisting of concerned citizens of the community. St. Paul-Ramsey Hospital Medical Center (SPRH), through the Department of Psychiatry, provides medical care services under contractual agreement between the Center and St. Paul-Ramsey Hospital and Sanitarium Commission.

Patient Status

Throughout Entire Program

During 41 months of program activity (August 1, 1970 to December 31, 1973) 321 patients have been formally enrolled in the program, 78 of whom being admitted in the 1973 calendar year. Data for the total patient population is shown in Table 1. Ethnically, whites of both sexes have applied and qualified for care in increasing numbers compared with blacks (178 vs. 135), with females more so than males (52 vs. 28).

Females continue with the program at a rate slightly better than males (45% vs. 42%). Black females continue with the program at a more favorable rate than males (36% vs. 29%); while the reverse is observed with whites (42% vs. 52%). The retention rate for all males has become more favorable, compared to the previous year—36 percent in 1972 and 42 percent in 1973. In contrast, the retention rate for females dropped from 48 to 42 percent in the same year.

Since the program began, a total of 244 additional persons have personally consulted the Center but were ineligible to be enrolled in the program. This group is highly represented by the occasional narcotic and polydrug users. They were assisted medically and vocationally by referral to other appropriate agencies to care for their concerns.

TABLE 1
Patents by Sex and Race
August 1, 1970 to December 31, 1973

		Males			Females	
	Admitted	D/C'd	Active	Admitted	D/C'd	Active
Black	107	76	31	28	18	10
White	126	58	68	52	25	27
Indian	1	1	0	4	3	1
Other	3	2	1	0	0	0
Totals	237	137	100	84	46	38

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[*] St. Paul Drug Rehabilitation Center, Inc. and Department of Psychiatry, St. Paul Ramsey Hospital, St. Paul, Minnesota.

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[‡] Executive Director, St. Paul Drug Rehabilitation Center, Inc. Supported in part by the Medical Education and Research Foundation-SPRH, Grant No. 801D61.

For Calendar Year 1973

At the beginning of the 1973 calendar year, as shown in Table 2, there were 97 patients under care. Of these 38 (39%) were still under care at the end of the year and another 26 (26%) were discontinued and later readmitted and still under care. Hence, 64 (65%) of this group at the end of the calendar year are under care.

There were 78 new applicants during the year who were not previously treated in the program. Forty-nine (62%) of these new applicants are still under care at the end of the year and an additional eight (10%) were discontinued but were readmitted during the year. This represents a retention rate of 73 percent. There were 21 patients who applied to enter the program who were previously treated prior to the calendar year. Of these, 17 are still under care (81%) and four have been discontinued.

The 138 patients continuing participation in 1973 have an age range from 18 to 73. There were 10 patients between 18-20 years of age; 69 between 21-29; 37 between 30-35; 19 between 36-45; and three beyond 46 years of age.

A study of the occupational status in Table 3 shows that the 138 active patients during the 1973 calendar year improved their vocational status in increasing numbers, from 38 to 62 (27% to 44%). Unemployment dropped from 92 to 67 (66% to 48%). This is contrasted by the increased liability of unemployment among drop outs, from 130 to 145 (21% to 17%), shown in Table 4.

Of the 138 active patients, seven have attained more than two years of program participation, 30 over a year and less than two years, 64 between three months to a year and the remaining 37 patients are under three months. Some characteristics of the 37 patients in the program who have a year or more of participation shows the following: 21 are residents of the St. Paul area, 13 from Minneapolis, and the remaining three reside outside of the Twin Cities. Twenty-one patients in the group are employed, 13 unemployed, and three in school. Four of the seven patients who have more than two years of participation are either on probation or parole. There are eight

TABLE 2
Census of Patients—1973

		No. Still Under Care—year end	No. Discharged/Transferred to Other Types of Programs Not Readmitted	Readmitted—under care	Discharged and Readmitted—no longer under care
No. under care at beginning of year	=97	38	29	26	4
Admitted during year but not previously treated in this program	=78	49	10	8	1
Admitted during year and previously treated in program prior to past year	=21	16	4	1	0

TABLE 3
Employment Status of Active Patients

	Employed	Unemployed	School	Housewife	Totals at Report
Employed	26	34	1	1	62
Unemployed	10	52	2	3	67
School	2	6	1	0	9
Housewife	0	0	0	0	0
Totals at Admission	38	92	4	4	138

TABLE 4
Employment Status of Drop Outs

	Employed	Unemployed	School	Housewife	Totals at Termination
Employed	25	7	0	0	32
Unemployed	13	122	4	6	145
School	1	1	4	0	6
Housewife	0	0	0	0	0
Totals at Admission	39	130	8	6	183

of the other 30 patients with one to two years of program participation on parole.

Medical Considerations

During the 1973 calendar year 16 patients required admission to hospital for various causes: pancreatitis—one case; carcinoma—two; burns, 3rd degree—one; diabetes mellitus—one; gunshot wound—one; schizophrenia—one; headaches—one; pregnancy—one; heart disease—one; asthmatic bronchitis—one; cellulitis—one; hepatitis—one; overdose (other than methadone)—two; overdose (methadone)—one.

No hospitalization had been required for treatment of side effects or toxicity of methadone except for the single case of overdosage with methadone. The cases of cellulitis and hepatitis were observed in patients with prior and continuing history of such difficulties attendant with irregular heroin use. Methadone related medical problems per se have not been observed to militate against the use of the drug.

Evidence of occasional continued drug abuse is documented through weekly random urine collection and testing for morphine from each patient under direct monitoring. Accurate and rapid urine testing is done through Pharm-Chem Laboratories at Palo Alto, California. A survey of the last eight weeks of 1973 revealed: negative morphine ("No Chipping")—two months or more—80 (57.9%); occasional positive urinalysis for morphine—monthly or less—16 (11.5%); and frequent positive urinalysis for morphine—more than once per month—11 (7.9%). There were 31 patients who had been in the program less than two months.

Dosages of methadone range from five mgm. to 100 mgm. with only four patients requiring 100 mgm. doses. Those patients continuing in the program averaged 46 mgm; those terminated averaged 32.0 mgm; and those voluntarily detoxifying averaged 32.4 mgm. There were 17 patients that were on a detoxification schedule. Eleven of these patients were returned to maintenance and the remainder have discontinued program participation.

Discussion

Methadone physiologically alleviates narcotic craving and creates a cross tolerance state that reduces the addict's ability to experience the effects of heroin. Contemporary successful management of narcotic addiction, however, depends not only on what methadone can chemically do, but also on what support services are provided to enhance the optimum management of the addicted person. The drug develops a dependent state that facilitates a program of social, educational, and vocational rehabilitation. While methadone is effective, the search for superior chemicals and the extensions of the health care delivery system continues.

The St. Paul Drug Rehabilitation Center in concert with the Department of Psychiatry at SPRH is participating in a study to investigate the efficacy and safety of a longer acting methadone-like agent L-Alpha-Acetylmethadol (LAAM). LAAM has prolonged action and would offer the following distinct advantages over the use of methadone as a maintenance drug for heroin addicts: (1) less likelihood of illicit diversion due to the elimination of take home dosages: (2) greater convenience to patients affording them a more favorable opportunity for rehabilitation, and (3) reduced administrative costs for treatment programs. The project is sponsored by the Special Action Office For Drug Abuse Prevention (SAODAP) and is being conducted by 16 other methadone maintenance programs across the United States.

Narcotic addiction causes severe social as well as medical complications. As such, a combination of medical and social modalities is crucial in any treatment program. The observations in this survey show that continuous program participation promotes gainful employment and its consequence of reducing the criminal activities of the narcotic addict. Individual reports among participants reveal less subjective distress and less impairment in social effectiveness and function. The support services provided by the Center staff are invaluable in creating and sustaining an improvement in life style. Further extensions of the Center services have now been developed, addressing itself to the polydrug user, the occasional heroin user and a "drug free" program.

Summary

The center involved is community based with contractual links to a large medical facility. A high participant retention rate, low "street drugs" usage by clients and growing community acceptance have been attained. The observation that collaborative efforts between community resources and medical services are vital and essential for the successful management of the opiate addict is emphasized.

References on page 881.

Continuing Medical Education

November

Mayo Clinic

In Rochester

Otolaryngology for the Generalist

November 2, 1974—Mayo Clinic—Contact: Mr. W. L. Nietz, Mayo Clinic

Clinical Reviews

November 4-6 and November 11-13, 1974—Mayo Clinic—Contact: Mr. W. L. Nietz, Mayo Clinic

World Congress of Dyslexia

sponsored by Orton Society in cooperation with Mayo Foundation

November 7-10, 1974—Mayo Civic Auditorium—Contact: Mrs. Paula Rome, 712-289-1532

Outside Rochester

Waconia Medical Seminars

November 7-8, Waconia, Minnesota—"Thyroid Problems"—Contact: Charles V. Carlson, M.D., Mound, Minnesota.

Faribault Medical Seminars

November 9, Faribault, Minnesota—"Infectious Diseases"—Contact: Roy H. Good, M.D., Faribault Clinic.

Owatonna Medical Seminars

November 11, 1974, Owatonna, Minnesota—"Lupus Erythematosis and Rheumatoid Arthritis"—Contact: Mr. Howard Place, Owatonna City Hospital.

Southern Minnesota Academy of Family Physicians

November 19, Mankato, Minnesota—"Diabetes and Obesity in Children," Contact: Roy H. Good, M.D., Faribault Clinic.

Mankato Medical Seminars

November 23, Mankato, Minnesota—"Suturing the Common and Uncommon Hand Lacerations"—Contact: J. F. Eckert, M.D., St. Joseph's Hospital.

Goodhue-Wabasha County Medical Seminars

November 25, Lake City, Minnesota—"Epilepsy" (Pediatric Neurology). Contact: D. W. Sontag, M.D., Lake City.

University of Minnesota

Registration information: Office of Continuing Medical Education, University of Minnesota, Box 293, the Medical School, Minneapolis 55455, or by phone (612) 373-8089.

Courses offered are:

November 6-8—*Principles of Colon and Rectal Surgery*

Surgeons and family physicians who provide surgical treatment for colon and rectal conditions will find this review and updating of surgical and management techniques of value. Video-tapes will be used to illustrate some of the procedures.

November 13-15—*Refraction for the Non-Opthalmologist*

This is a small and always over-subscribed course for physicians who want to learn eye refraction and add these services to their office practice. Applications received for waiting list only.

Twin City Urological Society

Pyelogram Conference, 6:00 P.M. on November 15, January 17, February 21 and March 21, at the Marriott Inn, Bloomington. All day spring seminar on April 19, also at Marriott Inn. Contact: Doctor A. S. Cass, St. Paul-Ramsey Hospital, St. Paul.

Metropolitan Medical Center

Neurology

Conferences, Fridays, 8:30 a.m., Center Building, Conference Room, 900 So. 8th St., Minneapolis. Contact: Mary J. Donner, Metropolitan Medical Center—338-7744.

Audio-Visual Network for Continuing Education

9:00 a.m. in Doctor's Lounge, second Tuesday of each month, 900 South 8th Street, Minneapolis. Contact: Margie Knutson, Metropolitan Medical Center, 338-7744.

Tumor Conference—Cancer

Every Monday except if a holiday. 12:00 noon, 900 South 8th Street, Lower Level Conference Room. Contact: Dr. Lyle J. Hay, MMC, 338-7744.

University of Iowa

November 8—Vascular Disease of the Lower Extremity. Auditorium 3, Level 3, Basic Science Building, Iowa City, Iowa. 6 prescribed hours by AAFP. Contact: University of Iowa, 101 CMAB, Iowa City, Iowa 52242.

November 8 and 9—Clinical Endocrinology Medical Alumni Auditorium (E-331), University Hospital, Iowa City, Iowa. Contact: University of Iowa, Iowa City.

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"In this age of specialization, there's a vital need for discussion of the broader implications of new-found knowledge. The 28th AMA Clinical is designed for that purpose. . .to bring together physicians of the various specialties to study and discuss the broader aspects of medicine as they apply to their practices."

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[1] *Demeulenaere, L.: Action du R 1132 sur le transit gastro-intestinal, Acta Gastroent. Belg. 21:674-680 (Sept.-Oct.) 1958.*

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Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and etropine ere secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoreticelly possible et high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be eddiction prone or having a history of drug abuse. The subtherapeutic amount of etropine is added to discourage deliberate overdosege; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism mey occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin end mucous membrenes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedetion, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, heedeche, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, gient urticaria and peralytic ileus.

Dosage and administration: ***Lomotil is contraindicated in children less than 2 years old.*** Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observetion should extend over at least 48 hours.

Dosege lorms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. *Liquid,* 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

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Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Possibly effective: For relief of upper respiratory tract congestion and hypersecretion associated with vasomotor rhinitis and allergic rhinitis, and for prolonged relief.

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Final classification of the less-than-effective indications requires further investigation.

Contraindications: Hypersensitivity to any component; concurrent MAO inhibitor therapy; severe hypertension; bronchial asthma; coronary artery disease; stenosing peptic ulcer; pyloroduodenal or bladder neck obstruction. Children under 6.

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Usage in Pregnancy: In pregnancy, nursing mothers and women who might bear children, weigh potential benefits against hazards. Inhibition of lactation may occur.

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Precautions: Use cautiously in persons with cardiovascular disease, glaucoma, prostatic hypertrophy, hyperthyroidism.

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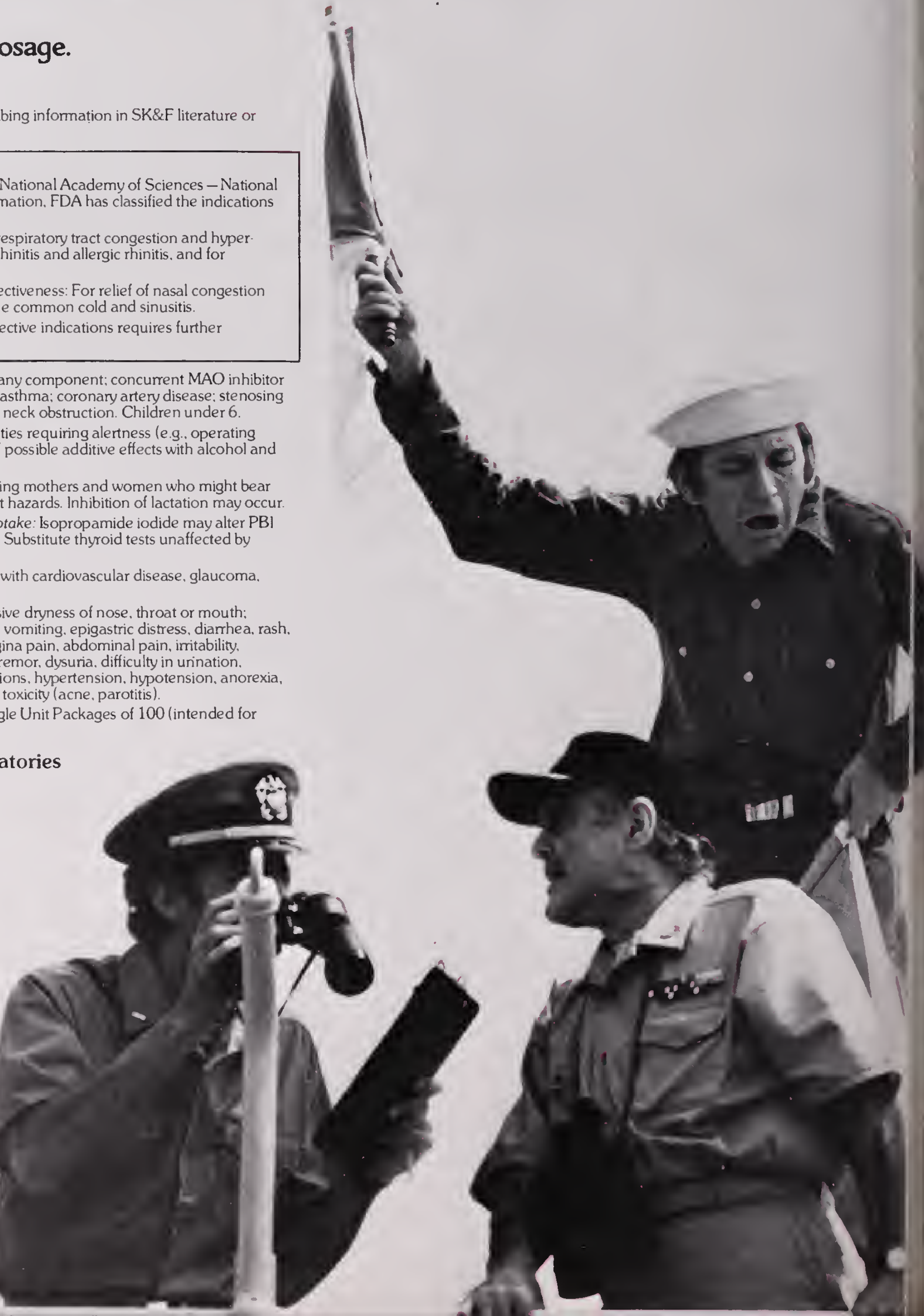


Editorials

Minnesota Medical Foundation

Medical Benefactor to the University of Minnesota

The November 1974 issue is contributed by members of the staff of the University of Minnesota Medical School, Minneapolis. As one of the guest editors and as Director of the Minnesota Medical Foundation (MMF), I am taking this opportunity to describe the organization for the readers of Minnesota Medicine.

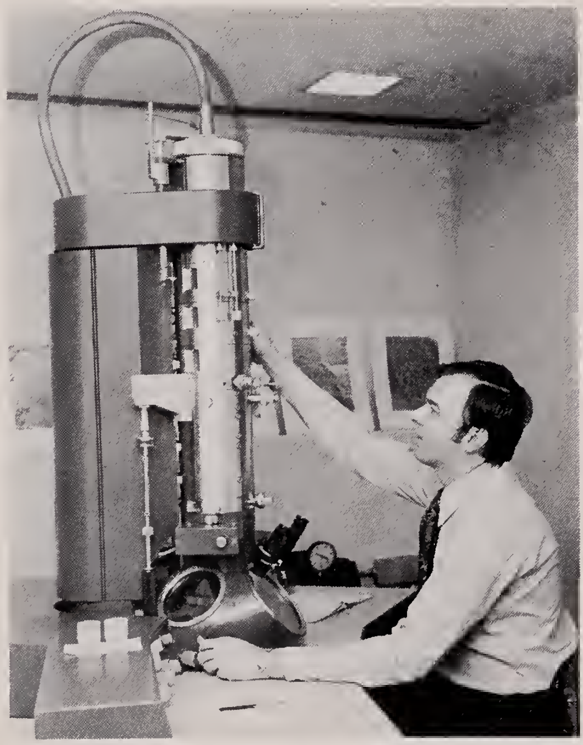
Medical research and education programs of the University of Minnesota get a million dollar lift each year from the MMF. The Foundation is a non-profit corporation, separately chartered from the University, but with support of its medical schools as its sole purpose for being.

The Foundation was created in 1939 by a group of medical alumni and faculty of the University who saw an increasing need for private financial support of medical education and research. Over the years the Foundation has grown dramatically until today it supports more than 100 research projects and has helped many hundreds of medical students finance their education. MMF's research grants are especially important as "seed money" for new research projects or beginning investigators. Recipients of MMF research grants frequently move on to much larger federal or private grants.

In addition to funding investigative projects, MMF also finances equipment and facilities for medical research, research professorships and fellowships for post-M.D. medical research trainees. Past MMF grants have been instrumental in recruiting skilled researchers and teachers for Minnesota's medical faculty.

MMF currently supports professorships in cancer research and urology. The Foundation owns the Stone Research Laboratories and leases them to the University. These facilities house the cancer and heart research laboratories of several medical school faculty members. In the past year the Foundation has loaned the University of Minnesota $110,000, about half of it interest-free, to help the institution remodel the interior of the Stone Research Laboratories to suit the needs of programs. MMF has financed three electron microscopes for Medical School laboratories, one of which is shown in the accompanying illustration.

Many of Minnesota's doctors received MMF aid while they were medical students. The Foun-



Dr. Robert E. Scott, pathologist, is shown using an electron microscope purchased and installed with a $75,000 Minnesota Medical Foundation grant to the University's Department of Pathology and Laboratory medicine.

dation gave its first medical student aid—five scholarships of $500 each—in 1949. Its medical student aid program for 1973-74 has grown to nearly a quarter of a million dollars. Most of MMF's medical student aid is in the form of long-term low-interest loans. Well over half of all past scholarships have been voluntarily pledged back to the Foundation by the recipients. This quid pro quo system has been promoted by the Foundation to help guarantee the future of the Foundation's student aid programs. MMF also operates an emergency short-term loan service for medical students who have cash flow problems. The emergency loans offer up to $300 interest-free for 90 days. Last year the Foundation gave 297 emergency loans totalling $73,466. Most went to medical students, with a few going to interns and residents. Since the first emergency loan in 1959, MMF has issued more than 3,000 of these short-term loans, totalling well over half a million dollars.

The first short-term emergency loan program of the Foundation was started in 1959 with establishment at MMF of the Dr. Herman M. Johnson Memorial Loan Fund of the Minnesota State Medical Association. The Fund was started with a grant to MMF from the State Medical Association of $5,000. Later, another $5,000 was added to the revolving loan fund by the association. Since the inception of the Johnson Loan Fund the $10,000 investment of the State Medical Association has meant 2,524 interest-free short-term loans to students, totalling $411,335. Of the 297 short-term loans handled by the Foundation in its last fiscal year, 126 loans totalling $26,110 were issued through the Herman Johnson Fund.

The Foundation's programs are timely and flexible. In support of graduate medical education in 1973, MMF picked up $75,000 in post-M.D. medical research traineeships when federal support was lost.

When the University's Board of Regents agreed to make a million dollars available to lend students the difference between 1972 and 1973 tuition (increases of nearly 60 percent for medical students), MMF guaranteed $30,000 to pay the seven percent interest for medical students hard hit by the tuition jump.

MMF made a $250,000 interest-free loan to the University in 1973 to help with construction costs of the new Cardiovascular Research and Training Center.

MMF also conveys several honors which recognize excellence in research, teaching and student performance. MMF's Distinguished Teaching Awards have provided annually since 1962 a coveted honor, including $1,000 cash prizes, for Minnesota's finest medical teachers. The Minnesota State Medical Association co-sponsored the teaching awards with MMF through 1972 and until then provided the cash prizes. Student Achievement Awards, also carrying $1,000 cash prizes, were introduced by MMF in 1971. The Foundation provides several other awards for excellence each year.

Eivind O. Hoff*
Guest Editor

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*Executive Director, Minnesota Medical Foundation, Box 193, University Hospitals, University of Minnesota, Minneapolis, Minnesota 55455.

Obscured Hills

THIS FALL THE trees of Minnesota exploded into their brightest colors in years. Perhaps it was our early frost.

This glorious yearly demonstration of the cycle of life is symbolic of health. As the leaves fall each year they lay bare the shapes of the hills allowing us to see the land that sustains our lives.

Each tree differs from other trees as the articles in a medical journal differ. Both need nourishment.

Fall is a fitting time for the readers of MINNESOTA MEDICINE to peer through and beyond the varied writings to observe the structure beneath. A close look into this University of Minnesota edition will reveal some hills obscured by the leafy woods of our Spring issue.* The Minnesota Medical Foundation has often been the hidden earth mother to the growth of our medical writers.

There are few self-made men and even fewer self-made clinical investigators. I can recall ask ing an elderly patient if she wasn't very proud of her two successful sons. She said, "Yes, but don't forget that it was their mother's money that got them started."

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*July, 1974 issue of Minnesota Medicine.

In this November MINNESOTA MEDICINE you will find everything from sex to RNA viruses, adolescence to dislocation and transplantation to psychiatry (a good pair). You can be proud of them all but don't forget that it was their mother's money that got them started.

John B. O'Leary, M.D.
Guest Editor

What's New in the KUB Tract

TO THOSE NOT entirely familiar with what is going on in renal transplanation the paper from Najarian's group* presents some startling statistics. The largest renal transplantation center in the world is now centered in the University of Minnesota Hospitals. No reported large series of renal transplantation has had better survival statistics.† Patients with renal failure, with many contraindications which recently precluded transplantation, are now accepted for this surgery, including patients of advanced age up to 72 years.

Renal transplantation and dialysis have become major clinical modalities at Minnesota with over 100 transplantations now being done yearly. This alone is a great factor in the excellent results achieved since proficiency in this extremely complicated medical and surgical problem can only be gained by experience.

The results given in the figures and tables of surviving subjects should be interpreted in the light of the dismal results that would be expected from therapy other than dialysis and transplantation.

Fraley et al.‡ report on a virus with an RNA core associated with transitional cell cancer (TCC), one of the oncoRNAviruses. Starting with fresh human surgical specimens of TCC, they have shown this tissue contains virus-like particles which resemble oncoRNAviruses which cause some animal cancers.

To fulfill Koch's postulates, to reproduce the disease, TCC, by introducing into the host a virus of the same species, is not an option available to investigators. But if the virus is indeed etiologically related, new vistas of diagnosis and treatment appear in this most important of urological tumors.

Reuben Berman, M.D.
Editor

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*See page 886.

†J. Najarian personal communication.

‡See page 871.

Annual Meeting

The Minnesota State Medical Association's annual meeting in St. Paul, May 21-23, 1975, at the St. Paul Hilton Hotel.

Letter to the Editor

Dear Editor:

May I offer a slight modification to an otherwise fine article by Dr. Reynold Jensen in the special issue on Aging, August 1974.*

The Protective Services undertaking of Ebenezer Society has not been discontinued. The federal grant (channelled to us by the Minnesota Governor's Citizens Council on Aging) of Title III funds under the Older Americans Act was continued for an unusual fourth year, through June 30, 1974. Ebenezer Society has repeatedly indicated that the program will be continued under Ebenezer auspices, and is in fact doing so at the present time. Additional funds from other sources are certainly needed and will be welcomed, as during the period while Ebenezer is doing the job unaided for the entire community, it has perforce had to become a somewhat smaller program.

Ebenezer Foundation is currently trying to build up an endowment, via bequests and gifts, for the purpose of providing a permanent capital base for such a private agency alternative to the public welfare system. Incidentally, in addition to Dr. Jensen's mention of "a creditable demonstration of need," the Ebenezer Protective Service program is proud of having demonstrated techniques for other social agencies to use in dealing with deteriorated, confused elderly, and is also proud of having developed, with the cooperation of the county judges of Minnesota, new legislation on conservatorship (state law since August 1, 1973) which enjoyed unanimous passage by both houses of the 1973 Minnesota legislature.

For several years, county welfare departments have been the *designated* agency in all communities of Minnesota for handling the confused aged. Communities with more complex problems, such as the metropolitan areas, really do stand to benefit, however, from the continuing availability of an alternative, non-welfare program under private auspices.

Edward L. MacGaffey, Ph.D., ACSW
Director, Ebenezer Society Community Services

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*Page 611.

Cover Photo

"Winter Solitude"

The photograph was taken on Christmas Eve, 1971, on Dr. Richard A. Carlson's father-in-law's dairy farm, which is located near Northfield, Minnesota. The buildings in the background are those of the neighboring farm. The tracks in the snow in the foreground were made by a wild animal of some sort.

The camera used was a Minolta SRT101 with a 55mm lens. The film used was Kodachrome II. Unfortunately, no record of the exposure factors used was kept.

Dr. Carlson is currently in the second year of Radiology residency at the Mayo Clinic. A native of Lindstrom, Minnesota, he graduated from the University of Minnesota Medical School in June, 1972, and served a Medicine Internship at the Mayo Clinic.

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Adolescent Patients as Adults

WENTWORTH QUAST, PH.D.,* A. JACK HAFNER, PH.D.,*
and MICHAEL J. SHEA, PH.D.†

The adult adjustment of 1000 former adolescent psychiatric and pediatric patients: a twenty-five year follow-up; some preliminary findings.

THE PURPOSE OF THIS RESEARCH is to study the adult outcome of former adolescent patient groups. For the primary study group a sufficiently large group of psychiatrically disturbed adolescents were chosen to insure a representative sample of psychiatric problems of adolescents. For comparative purposes a group of adolescent pediatric patients without psychiatric problems was followed. Adult outcome for both groups was determined by personal contact, psychological testing and use of agency records.

Subjects

The population for the study was 1112 former adolescent patients, ages 13 through 17, seen at the University of Minnesota Hospitals during 1938-1950. Physicians throughout the state of Minnesota were often the original source of referral. At the time of the follow-up contact (21 to 33 years later) the youngest patient was age 38 and the oldest, 46. Thus, sufficient time elapsed from adolescence to adulthood to assure that we were truly sampling adult outcome.

The Child Psychiatry Unit at University of Minnesota Hospitals was organized in 1938. Starting from that date, historical, psychological, and medical data were obtained on 869 consecutive, white male and female adolescent patients referred to Child Psychiatry at the University Hospitals. A contrast group of 243 non-psychiatrically disturbed patients was chosen from the Department of Pediatrics. Each of these patients was matched with his psychiatric counterpart according to age, sex, and date of referral. Patients were excluded from the non-psychiatrically disturbed pediatric group if they carried a diagnosis of brain syndrome or mental deficiency since these diagnoses are classified as mental disorders according to the American Psychiatric Association Diagnostic Manual. Pediatric patients were also excluded if behavior problems during adolescence were apparent in the medical charts or if repeated or serious acts of delinquency were entered in police records. The total subject population for our study included both in-and outpatients and was found to be very representative of the state of Minnesota with respect to factors such as socioeconomic status, geographic location and population density of residence, religion and others.

Method and Data Collection

The University Hospitals' medical records of our subjects were found to be adequate, including histories, physical examinations, laboratory studies, consultation evaluations by specialists such as audiologists, speech therapists, neurologists and neurosurgeons, allergists, and endocrinologists. These records also included outside data from sources in the community such as schools, public welfare and social agencies, and case summaries. Outpatient records also contained a summary document containing similar information. For the psychiatric group, in addition to psychiatric histories, evaluations, and treatment notations, most records contained social histories and comprehensive psychological and physical examinations.

Recognizing the unreliability of psychiatric diagnoses, a global mental health rating was made on each patient utilizing all information available. Similar mental health ratings were made from information available at adulthood, and a separate rating made for the interim period between adolescent and adult contacts. These mental health ratings made for both patient groups were classified in terms of five categories ranging from positive mental health to incapacitating mental health problems. This classification was based on a global judgment made by experienced clinical psychologists using a combination of various sources of information including medical records, interview and questionnaire data, psychological test data, and public agency record information.

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*Division of Health Care Psychology, Division of Child and Adolescent Psychiatry, Department of Psychiatry, University of Minnesota Medical School.

†Hennepin County General Hospital and Division of Health Care Psychology, Department of Psychiatry, University of Minnesota.

Support for this research was, in its inception, from a small grant from the Graduate School of the University of Minnesota, followed by a large grant from the National Institute of Mental Health (MH 12038). More recently, funds for data analysis have come from the Division of Child Psychiatry, Department of Psychiatry, University of Minnesota and the research section of the Department of Psychiatry, University of Minnesota.

Purposes of Study

The general aims of this study are fourfold:

a. To compare the adult mental health status of former psychiatrically disturbed adolescent in- and outpatients with that of their non-disturbed patient peers.

b. To determine the extent to which the degree of adolescent mental health and type of adolescent problems are correlated with adult mental health for the same individual.

c. To determine the relationship of demographic variables to adult mental health for both adolescent psychiatric and non-psychiatric patient groups.

d. To assess the significance of adolescent interpersonal relationships (parent-child, sibling, peer, and parent-parent) to the adult mental health of psychiatrically disturbed adolescents.

The importance of this research follow-up lies in its providing a more precise understanding of the adjustment problems in that acute phase in human development—adolescence—and in its help in determining whether degree of disturbance in adolescence has long-term consequences. This kind of information should increase the accuracy of predictions made from certain adolescent adjustment factors, historic data, and test performances. Factors common to normal adjustment of previously maladjusted individuals can be isolated. These data should also contribute to a more precise formulation of psychiatric classification and treatment for adolescents than now exist, and to suggest prophylactic measures that can be instituted early.

Of the total subject pool of 1112, we located 057 subjects (95%). Of this group, 100 were dead, 33 before age 21. For the rest of the located subjects, 73% were in the general Minnesota area and 27% outside of this area.

Regarding the actual response rate for the 057 subjects of the 1112 subjects that we were able to locate, interviews or questionnaires were completed on 950 of our subjects, a response rate of 93% of all located subjects. Fifty subjects (5%) of all located subjects refused to take part in our study. We were unable to obtain interview information from another 24 (2%). The return rate of our MMPI's was 76% of the participating subjects. An unexpected source of subject data were letters that subjects sent us accompanying the MMPI containing reflections about their adolescent contacts at the University Hospitals, and requests for help to deal with current adjustment problems.

Studies Completed

The primary analysis of data on the entire Adolescent Follow-Up Study population is still in progress. A number of sub-studies have been completed, however, on varied topics utilizing selected samples of subjects. Some of the findings of these studies are the following:

Methodologically, because it was not feasible to interview persons living at a great distance it was learned through a sub-study that a mailed, self-administered structured questionnaire was highly correlated with and as useful as a personally conducted interview.[1]

Regarding children at risk for developing serious adjustment problems in adulthood and a search for the antecedents of those problems, another sub-study of adolescents with symptoms of antisocial, acting out, externalizing behavior versus a sample with overinhibited behavior clearly demonstrated the vulnerability to adult psychopathology of those deviant adolescents whose symptomatology is marked by "turning against others." A contrast group of non-psychiatrically disturbed pediatric patients made the best adult adjustment. Some of the antecedents in family pathology of the "externalizers" (antisocials) were: Fathers showed a heightened incidence of alcoholism, greater job instability, and absence from the home. Mothers of "externalizers" showed a greater incidence of mental disorders than mothers of "internalizers" (overinhibited). Parents of "externalizers" showed marked marital conflict and "externalizers" had markedly poorer relationships with their mothers.[6]

In early childhood "externalizers" suffered severe trauma, such as a number of foster home placements, had a history of school problems, and had poor peer relationships. In adulthood they were more generally disturbed than the "internalizers," showing correctional records, high divorce rate and low occupational levels.

Another sub-study investigated the prognostic value of different methods of classifying adolescent psychiatric patients. Findings were consistent with the existing literature which has shown that adolescents with neurotic symptomatology had a better adult outcome than those with psychotic symptoms. The study also showed that early diagnoses were of greater prognostic value with females than with males, especially when females were diagnosed as psychotic or personality disorder (a non-psychotic personality defect with social maladaptation). The best predictor to adult adjustment was severity of disturbance in adolescence.[2]

A study seeking to delineate the characteristics of severely disturbed adolescents concluded that such individuals are not likely to "outgrow" the problem present in adolescence but continue to have serious psychiatric and social problems as adults. It was also shown that prognostic variables such as parental absence from the home, poor relationships with siblings in adolescence, prior psychiatric or correctional contact, low IQ, duration of symptoms and others may be relevant as predictors only for certain periods in the life history of an individual, a finding that has implications for follow-up research as well as being a partial explanation for the inconsistent results now found in the literature.[4]

A follow-up of 33 adolescent schizophrenic subjects revealed that 17 to 30 years post University Hospitals contact 61% had a chronic course (i.e., spent at least ten years hospitalized for clearly diagnosed schizophrenia) while 39% had a more adequate adjustment, although frequently this was with neurotic-like deficits. These two outcome groups were compared on information available at the time of adolescent treatment contact. The poorer outcome patients were more likely to have relatives with chronic schizophrenia, a disturbed parent, below average intelligence, hebephrenic subtype diagnosis, and distinctive developmental changes involving a shift from an active antagonizing of other youngsters in childhood to withdrawn behavior with retreat into an active fantasy life.[5]

An investigation of the effects of father absence from the home on the children indicated that father absence interacts with age and sex. Father absence in childhood seems more harmful to boys relative to adult adjustment. Father absence occurring in adolescence seems to be more deleterious to the adult outcome of females.[7]

A study checking the stability of personality testing over time using the Minnesota Multiphasic Personality Test corroborated clinical experience that high clinical scale scores are not considered as indicative of serious psychopathology in an adolescent as they are in an adult. High scores in an adolescent are more likely to be interpreted as the result of situational stress, identity crises, etc. Over a 19-year test-retest period scores on five clinical scales showed a significant decrease from the period of adolescence to adulthood.[3]

The above findings are from sub-studies and the analysis of the data from the major Adolescent Follow-Up Study is still in progress. A book on the study will be forthcoming late in 1974 or early 1975.

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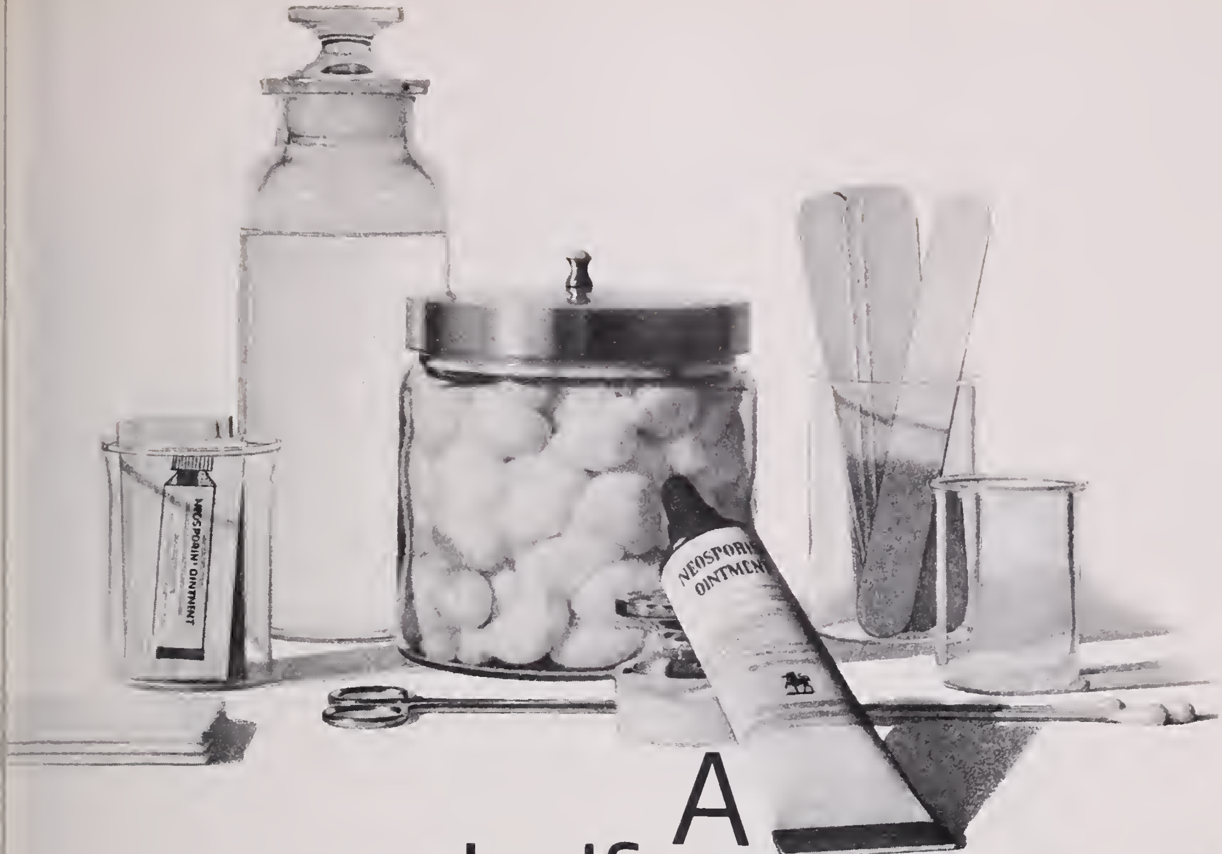

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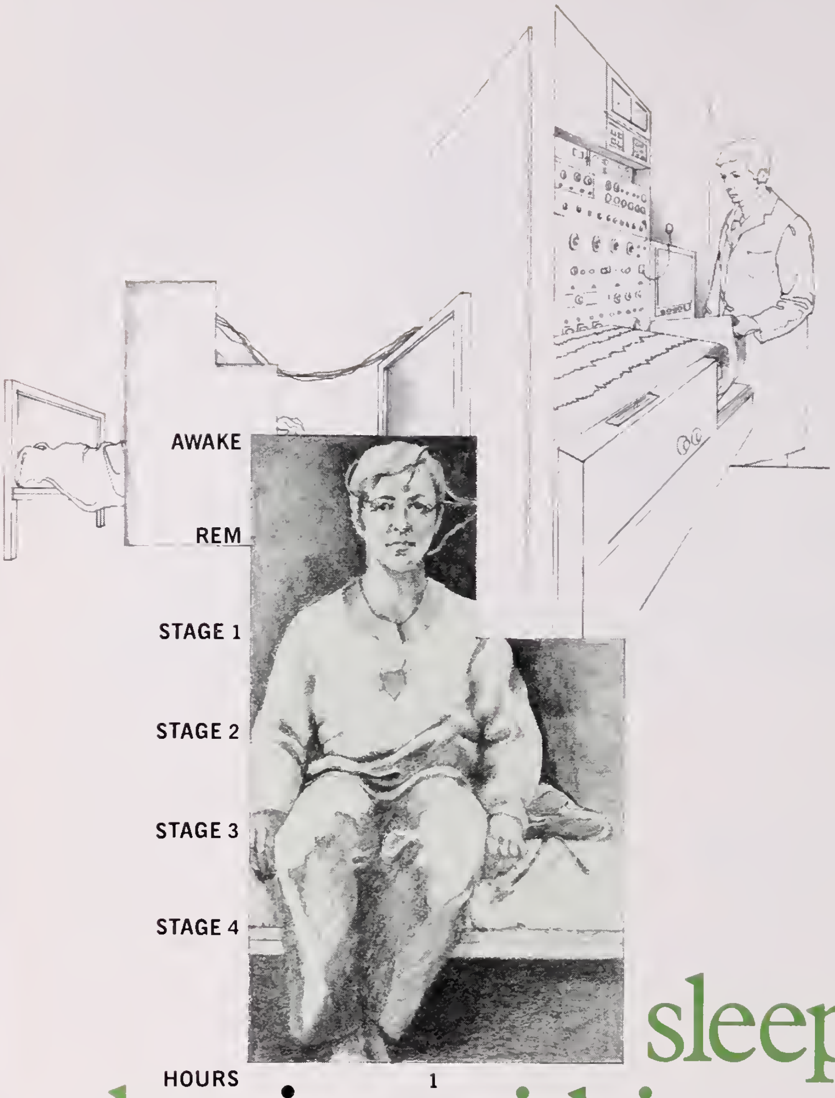

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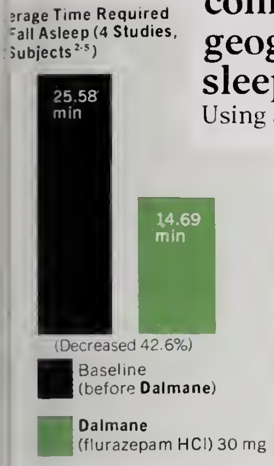

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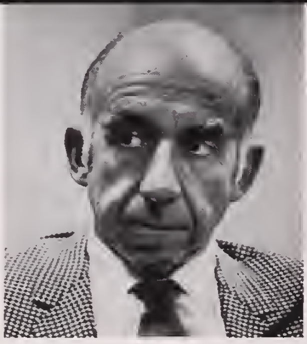

Dr. Jeremiah Stamler
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a great fund of information
it the drug products he is re-
sible for. He is usually able to
ver most questions fully and
ligently. He can also supply
nts of articles that contain a
t deal of information. Here,
exercise some caution. I usu-
ccept most of the statements
pinions that I find in the
rs and studies which come
the larger teaching facilities.
s without saying that a physi-
should also rely on other
es for his information on
nacology.

ing of Sales Representatives

Ideally, a candidate for the
ion as a sales representative
harmaceutical company
d be a graduate pharmacist
as a questioning mind. I don't
this is possible in every case,
o it becomes the responsibility
of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

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city they are indeed useful;
cularly in the fact that they
minate broadly based educa-
l material and serve not just
'ushers" of their drugs.

ther Side of the Coin

Obviously, the pharmaceuti-
mpanies are not producing all
naterial as a labor of love—
re in the business of selling
cts for profit. In this regard
nbitious and improperly moti-
sales representative can
a negative influence on the
icing physician, both by pre-
g a one-sided picture of his
ct, and by encouraging the
tioner to depend too heavily
gs for his total therapy. In
ways, the salesman has often
ted objective reality and
mined his potential role as an
tor.

dustry Responsibility

Since the detail man must be
ormation resource as well as
esentative of his particular
naceutical company, he
d be carefully selected and
thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.*, the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that information must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

*Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005*

P·M·A

Psychiatric Consultation in a General Hospital

JOHN M. SCANLAN, M.D.*

This study analyses the psychiatric disorders found in a general hospital and tries to provide a base of comparison with future studies by incorporating a standardized diagnostic classificatory scheme proven reliable in previous studies using larger numbers of patients.[1,2]

THE AVAILABILITY of psychiatric consultations has markedly increased within general hospital settings. Little has been published however regarding the types of psychiatric disorder encountered. A comparative approach to those studies is difficult due to the variabilities in diagnostic terminology and criteria.

Methods

The study was conducted in the Department of Psychiatry, St. Paul-Ramsey Hospital & Medical Center (SPRH). SPRH is a 611 bed city-county general hospital serving the St. Paul, Minnesota metropolitan area and is affiliated as a teaching institution with the University of Minnesota Medical School.

At the time this study was carried out one full-time faculty psychiatrist provided consultation for all adult in-patients. In addition, although not included in this study, consultation services were also available from the Alcohol and Drug Treatment Unit and the Child Psychiatry staff.

This report deals with all consultations (n = 170) done by the author during the period January 1, 1973 through May 30, 1973. The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*[3] was used to provide broad diagnostic categories. Final diagnosis, however, was based on "The Diagnostic Criteria for Use in Psychiatric Research" as described by Feighner et al.[4] A consultation report and diagnosis became part of the patient's record. Psychiatric and physical diagnoses used in this study are those from the initial consultation report.

Background

There were 4,310 patients admitted to SPRH (excluding psychiatry, pediatrics and newborn) during the five months of the study, distributed among the following clinical services:

Surgery	1,985
Medicine	1,157
OB-Gyn	658
Neurology	310
Alcohol & Drug	200
	4,310

The average age was 39 years, with an age range of 15 to 84 years. Sixty-six (39%) were males and 104 (61%) females. Marital status was as follows: 54 (32%) married; 57 (36%) single; 20 (12%) divorced; 16 (9%) widowed; and seven (4%) separated. Marital status was not known in 19 patients (11%).

Referring Services

Table 1 lists the five referring services. Subspecialties are included within Medicine and Surgery.

TABLE 1
Referring Services

Service	Number of Referrals	Percent of Total
Medicine	103	60%
Neurology	33	19%
Surgery	22	12%
OB-Gyn	9	5%
Alcohol and Drug	3	2%
Total	170	98%

The main reasons for requesting a psychiatric consultation are given in Table 2. "Treatment" refers to those cases where the primary physician

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*Assistant Professor of Psychiatry, University of Minnesota at St. Paul-Ramsey Hospital and Medical Center.

Supported in part by the Medical Education and Research Foundation—SPRH, Grant No. 801D81.

felt that there was, in addition to a physical disorder, a psychiatric condition requiring treatment. "Diagnosis" refers to those cases where a primary psychiatric disorder was suspected as the basis for the patient's physical complaints. "Placement" and "Competency" are self-explanatory.

TABLE 2
Reason for Referral

Reason for Referral	Number	Percent of Total
Treatment (Rx)	128	75%
Diagnosis (Dx)	37	22%
Placement (P)	2	1%
Competency (C)	2	1%
No Reason Noted	1	½%
Total	170	99½%

Primary Physical Diagnosis

Only the primary physical diagnoses of the 170 patients are included in Table 3. Secondary diagnoses, commonly found in combination with drug ingestions, alcoholism, the elderly, etc., are not included.

TABLE 3
Primary Physical Diagnosis

Primary Physical Diagnosis	Number	Percent of Total
Disease of the Central Nervous System	39	23%
Drug Ingestion (Overdose)	55	32%
Disease of Gastrointestinal System	13	8%
Disease of Cardiovascular System	10	6%
Disease of Metabolism	7	4%
Disease of Pulmonary System	9	5%
Disease of Genitourinary System	2	1%
nfectious Disease	5	3%
Laceration	1	½%
Fracture	5	3%
Pregnancy	6	4%
Miscellaneous	11	6%
None	7	4%
Total	170	99½%

Psychiatric Diagnosis

Table 4 lists the primary psychiatric diagnoses in the 170 patients. Twelve patients received more than one diagnosis: seven patients with ntisocial personalities also met the diagnostic criteria for drug dependency; two alcoholics had secondary organic brain syndrome and a third ne, a secondary affective disorder; one patient ad concomitantly OBS and a secondary affecve disorder; and another an acute OBS plus schizophrenia.

TABLE 4
Psychiatric Diagnosis

Psychiatric Diagnosis	Number	Percent of Total
Alcoholism	20	12%
Affective Disorder	17	10%
Conditions (Undiagnosed)	75	44%
Organic Brain Syndrome (OBS)	11	6½%
Schizophrenia	16	9½%
Hysteria	3	2%
Drug Dependency	6	3½%
Antisocial Personality	11	6½%
Mental Retardation	1	½%
Anxiety Neurosis	—	—
No Mental Illness	8	5%
No Psychiatric Diagnosis Made	2	1%
Total	170	100½%

Conditions where the consultant was unable to make a categorical diagnosis during the initial interview, using the research criteria were named "Undiagnosed" and accounted for nearly 50% of all consultations. The existence of significant psychological symptoms or behavioral disturbance in the psychiatrically undiagnosed cases is supported by the fact that 39 (52%) of these patients were admitted to the medical services because of a suicide attempt. The remaining "undiagnosed" cases exhibited one or more of the following features: depression, psychophysiologic symptoms, delinquent traits, severe marital problems, abuse of drugs and/or alcohol, or some type of personality disorder.

The *most* frequent psychiatric diagnosis was alcoholism (12% of the patients). In many of these patients the alcoholism was either unrecognized, or was not considered by the referring physician to be the primary diagnosis. One-third of these patients were admitted for drug ingestion, one-third for diseases of the central nervous system, and the remainder for complications related to alcohol ingestion. Thirteen patients were subsequently referred to the Alcohol and Drug Unit for treatment.

The 17 patients diagnosed as having affective disorders represent a conservative estimate for this category. A number of cases were classified as "undiagnosed" by criteria used for this study even though an affective disorder was strongly suspected. These patients were either transferred to the psychiatric in-patient facility or followed by the consultant for confirmation of the diagnosis, and treatment.

In most of the schizophrenic patients the diagnosis had been established by previous psychiatric admissions, in which case the psychiatrist was consulted to assist in the management of these patients admitted with primary physical problems.

The organic brain syndrome group did not include those patients admitted for drug ingestion, because a formal consultation was not conducted until the patients were over the acute effects ot the drugs. Patients ages ranged from 29 to 74 years, and the presenting syndromes were attributable to vascular, toxic, infectious, and metabolic disorders, and in one patient, to a brain tumor.

The ten patients with a diagnosis of antisocial personality were characterized by onset of delinquent behavior prior to age 15, plus repeated problems with school, family, job, and the law. Seven of these patients also met the criteria for a diagnosis of drug dependency, but it was considered as a secondary diagnosis since the onset of symptoms post-dated those of the antisocial personality.

Suicide Attempts

The 63 patients admitted for suicide attempts accounted for 37% of all consultation requests. Fifty-three of these attempts consisted of drug ingestion, and the remaining ten included: carbon monoxide inhalation, self-inflicted gunshot and stab wounds, and jumping from heights. Over a quarter of this group (18 cases) developed serious medical complications such as: blindness, hemothorax, multiple fractures, and coma.

A majority (39) of those cases attempting suicide were classified as having "undiagnosed" psychiatric conditions. Of the 24 remaining cases 19 were accounted for by the diagnosis of: affective disorder (six), antisocial personality (five), alcoholism (four), and schizophrenia (four). These 63 patients are being included in a larger group for closer study of suicide attempts admitted to this hospital.

Disposition

Thirty (18%) of the 170 patients were transferred directly to the psychiatric in-patient service. Main reasons for transfer included imminent danger to self or others, florid psychoses, and/or an inability to safely manage the patient in a medical ward or to sufficiently control the psychiatric disorder within the time confines of the need for hospitalization for the primary physical disorder. "Undiagnosed" conditions, affective disorders, and schizophrenia were present in 24 of the 30 transfers. Transfers to the Alcohol and Drug Unit are not included in this group.

Nineteen patients (11%) were followed in-hospital by the consultant utilizing psychotherapy, medications, and family therapy. Other patients were referred to various public and private treatment resources (social service agencies, mental health center, alcohol and drug treatment programs). Only ten patients (6%) refused to consider a treatment referral.

Summary

Psychiatric consultations on patients admitted to a general hospital over a five month period are reported. Study data was gathered prospectively and diagnosis was based on specific diagnostic criteria.

Significant psychiatric symptomatology was present in all but five percent of the consultations made. The largest percentage of patients were classified as having "undiagnosed" conditions under the diagnostic criteria used. The most frequent psychiatric diagnoses were alcoholism and affective disorder respectively. Twenty-nine percent required in-hospital psychiatric follow-up and another sixty percent were referred to outpatient treatment facilities.

The findings obtained here confirm the need for the availability of full-time psychiatric consulting services in a general hospital. Such services are an essential part of comprehensive in-hospital patient care.

Acknowledgment

The author acknowledges the assistance of Ms. Kay Kemp in the preparation of this paper.

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Sexual Attitude Reassessment

A Training Seminar for Health Professionals

JAMES P. HELD, B.Ch.E.[*]; CATHLEEN R. COURNOYER; CONSTANCE A. HELD[†]
and RICHARD A. CHILGREN, M.D.[‡]

An area of considerable concern to most physicians for which they are poorly prepared by training is human sexuality. The University of Minnesota Medical School has developed, with the co-operation of others, a new approach to human sexuality training for medical students, practicing physicians, and others in the health professions.

HUMAN SEXUALITY is an area of considerable concern to the physician as family and marriage counselor yet it is probably the area for which he is least prepared by education in medical school, internship and specialty training.

In their survey of California physicians, Burnap and Golden[1] found that the mean percentage of their patients who presented a sexual problem as their chief or ancillary complaint was 15.0%, varying from 1 to 60%. Physicians who routinely asked about sex problems encountered nearly twice as many patients suffering these complaints as those who only asked when it was indicated. Those physicians who displayed such signs of discomfort as blushing, fidgeting and looking away during the survey interview reported only one-fifth the incidence of sexual problems that the remaining physicians did. These results and the fact that 63% of the physicians reported that less than 1% of the sexual complaints had organic causes, indicate that the physician should be prepared to deal with sex problems. Most physicians considered dealing with sexual problems their responsibility, but 83% had had no formal training and 90% felt that more training was needed in this area.

Herndon and Nash's[2] survey of North Carolina physicians indicated that the only doctors who felt adequately trained were psychiatrists and obstetricians. Even with the increasing openness in discussing sexual matters that our society enjoys, the family physician is often the first to hear the sexual concerns of troubled adolescents and married couples. The physician needs more than a knowledge of anatomy and conventional counseling if he is to be comfortable and helpful in dealing with sexual problems.

A Human Sexuality Course for Medical Students

By mid-1970, the Medical School curriculum planners had accumulated extensive evidence both of patient need and of the lack of necessary educational training to prepare the professional.[3,4] Rev. Ted McIlvenna and his colleagues at The National Sex Forum, then a part of the Methodist Glide Foundation of San Francisco, now part of the Genesis Church and Ecumenical Center, had developed a two-day seminar on human sexuality that focused on feelings and attitudes. The Medical School Educational Policy Committee approved development of a two-day pilot program for key faculty, administrators, students and community leaders based on this model. After the pilot program all participants reported personal and professional benefits from the session and recommended that the program become an integral part of the Medical School curriculum.

In spring of 1971, three such two-day Sexual Attitude Reassessment (SAR) seminars were scheduled with volunteer medical students. They too reported personal and professional benefit, and recommended that it be a part of the curriculum.[5] Since then, three classes of second year medical students have participated in the semi-

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nars as part of their course work, as well as additional informational coursework on human sexuality. In December 1971, the Program in Human Sexuality was formed as a new academic and administrative unit responsible to the Dean of the Medical School. This program consists of an interdisciplinary faculty drawn from Medicine, Sociology, Social Work, Education, Counseling, Family Studies, Psychology, Public Health and Theology (from three Twin City area seminaries). It has adapted the SAR for research and training with other groups ranging from Physical Medicine and Rehabilitation (PM&R) professionals to adolescents and their parents. Seminar attendance is not restricted to medical students and spouses; other professionals, clergy, students, and others, have constituted a large portion of the over 5000 participants.

The Sexual Attitude Reassessment Seminar

The objective of the SAR seminar is to provide the participants with an opportunity to increase their understanding of their own sexuality and its importance in forming their attitudes toward the sexuality of others. The SAR process is based on the assumption that sex and sexuality are natural functions, that we all have the right to know about the range of human sexual behavior and to be acquainted with current information about sexuality, that we all have a right to our own beliefs and convictions, and that sexuality is an integral part of every personality; it is expressed in all that we do. We also assume that those in the "helping professions" (doctors, clergy, social workers, etc.) can more effectively assist clients with their sexuality when they understand and accept their own. We define sexual health to be the integration of the intellectual, emotional, and physical aspects of one's sexual nature to the enhancement of personality, communication, and love.

Large group discussions, media, and small discussion groups are the three major elements of the seminar. Each seminar has from 60-90 participants who meet together in a large room, furnished informally to enhance relaxation and comfort. Here they are given information by the discussion leader and are exposed to slides, films and audio-tapes. The slides and films explicitly depict sexual activity, and at one point several screens are used simultaneously to show the wide range of sexual behavior.[6] The films are concerned with many different aspects of sexuality, enabling participants to explore the physical, emotional, and intellectual components of sexual health.

Several times during the seminar the participants form smaller discussion groups of about a dozen people, which foster individual expression of feelings and thoughts about the different aspects of sexuality presented in the large group discussions and media.

During the first day of the seminar the topics of fantasy, masturbation, sexual variation, and the wide range of sexual behavior are introduced and discussed in the large group. Following the introduction of these general topics, the small groups meet to share their feelings on a more personal level. Meals and coffee breaks are included in the process to avoid interrupting involvement with the seminar. On the second day segments concerning relationship aspects of sexuality, body image, male and female roles, and sexual enrichment are presented. Additional days are often included and have a special focus, e.g. disability. Upon the SAR's conclusion, participants are requested to evaluate their experience and are provided with both a comment sheet and a more structured questionnaire.

Participant evaluation gives feedback to the small group discussion facilitators, the large group

TABLE 1

Immediate Post Seminar Evaluations by Participants in 1973 Seminars*

	Physicians (N = 93)		Nurses (N = 103)		Medical Students (N = 178)		Clergy (N = 49)	
	Yes	No	Yes	No	Yes	No	Yes	No
Did you personally find this seminar beneficial?	96.8%	3.2%	95.1%	4.9%	93.2%	6.8%	100 %	0 %
Do you think this seminar should be a required part of the training for your profession?	89.2%	10.8%	86.4%	13.6%	80.0%	20.0%	91.7%	8.3%

---

*Includes two-day, three-day and seven-day workshops. 96% returned questionnaires.

leaders and the media coordinators, helping to constantly improve the seminar. In 1973, 96% (1381) of the participants evaluated the seminar. Ninety-five precent of respondents found the seminar beneficial, 94% found it enjoyable and 92% said it helped them, at least somewhat, to discuss sex more freely. Nearly 90% of the 93 physicians and 86% of the 103 nurses who participated said they thought the seminar should be a required part of the training for their professions, and 89% of the physicians said it enabled them to discuss sex more freely.

Some of the participants' comments indicate professional effects of the seminar such as, "I was somewhat apprehensive about examining male patients . . . Now I feel I can deal better with sex questions and if a male does have an erection while examining him, how to deal with it." Other comments refer to an increased understanding of other people's sexuality and the problems of sexual minority groups: "I have clarified many things— I feel more comfortable with homosexuality now . . . feel more understanding about the handicapped and sexual feeling," "I can relate to my children easier." Most of the comments, however, refer to personal insights and beneficial changes in the participants' sexual relationships. One person said, "I have a more definite loving feeling about my wife," another said, "It opened my partner and myself to greater communication, it helped my thinking about my own personal problems." A common comment was "I realized that other people have the same problems in sex that I do," though one person said, "I was hoping I wouldn't be alone on all my hangups but found I was."

Of the 920 participants who attended the seminar in the Fall of 1972, 60% (552) returned a six-week followup questionnaire. In response to questions about the benefit of the seminar, 90% found the seminar beneficial, 61% experienced a change toward more comfort in their non-sexual behavior, and 50% felt their sexual behavior had changed toward greater satisfaction. Thirty-eight percent of the respondents experienced no non-sexual behavior change and 50% did not feel their sexual behavior had changed. One year after the seminar, the participants were sent another questionnaire. Of the 327 participants who returned both followup questionnaires, 86% thought the seminar was personally beneficial and 88% felt the time and expense of attending

TABLE 2

Immediate Post Seminar Evaluations by Participants in 1973 Seminars*

	Physicians (N = 93)			Nurses (N = 103)			Medical Students (N = 178)			Clergy (N = 49)		
	yes %	somewhat %	no %	yes %	somewhat %	no %	yes %	somewhat %	no %	yes %	somewhat %	no %
As a result of this seminar do you think you can discuss sex more freely with others?	63.7	25.3	11.0	72.5	23.5	3.9	59.3	30.5	10.2	77.1	18.7	4.2
Do you think this seminar accomplishes our goal of dispelling myths about sex?	62.0	34.8	3.3	64.7	32.4	2.9	50.8	39.5	9.6	73.5	26.5	0.0

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*Includes two-day, three-day and seven-day workshops. 96% returned questionnaires.

TABLE 3

Immediate Post Seminar Evaluations by Participants in 1973 Seminars*

Please indicate the effect on you of each of the following aspects of the seminar.	Helpful	(N=1381) No Effect	Harmful
Small group discussion	87.4%	11.3%	1.3%
Large group discussion	79.8%	20.0%	.2%
Movies	92.6%	6.2%	1.2%
Music	72.8%	24.3%	3.0%
Slides	74.0%	24.9%	1.1%

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*Includes two-day, three-day and seven-day workshops. 96% returned questionnaires.

the seminar were worthwhile. Sixty-six percent said their non-sexual behavior had changed toward more comfort, 54% said their sexual behavior had changed toward greater satisfaction, 33% had experienced no lasting change in their non-sexual behavior, and 45% felt their sexual behavior had not changed.

Discussion

These evaluations and personal comments from participants, coupled with our experience, have shown us several important things about the seminar. The small group discussions are very helpful for the integration process of the participants and in this regard it is essential to have open, responsive, comfortable group discussion facilitators. For this reason, training the leaders to deal with sexuality without embarrassment, and with openness and an understanding of and comfort with their own sexuality has been necessary. We have also found that the use of sexually explicit films is of great importance in enabling each participant to form a clear idea of what types of sexual behaviors other people engage in, to help him face his own reaction to such behaviors, and to allow him to deal more comfortably with his own reactions to the subject matter. In order to promote the exploration of each participant's attitude we have found it important to provide a relaxed, comfortable, nonjudgmental setting for discussion.

The seminar has been used as the basic component of several training experiences tailored to the needs of seminary students, clergy, staff from Minnesota State Hospitals, and counselors and patients in physical medicine and rehabilitation. The programs have been successful in increasing most participant's comfort in dealing with sex on a personal and professional level.

In seminars that focused on physical disability, professionals commented that the seminar would improve and increase the frequency of their sexual counseling.[8]

In commenting on personal benefits from the SAR, participants cited increased communication on a sexual and non-sexual level with their partners, a deeper awareness of their own sexual feelings, and more understanding of other people as individuals. Similarly, a seminar tailored for adolescents and their parents produced increased understanding between them about their values and beliefs in both sexual and non-sexual areas.[9] Because the seminar helps increase communication and provides a focus on sexuality, therapy groups were started using the seminar as an initial group experience. The seminar helped the groups deal more readily with sexuality, as well as providing an important information base for the clients.[10]

Summary

We think that an attitudinal approach to sex education is valuable for those in medicine and the other health professions, as well as for those who seek sex education for purely personal reasons. The exploration of one's own feelings and attitudes is a requisite for effective counseling in the sexual area; it is obviously a path to better understanding of other people. Through the Sexual Attitude Reassessment seminar, we try to facilitate this exploration.

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(Continued to page 933)

The more physicians consider the hemodynamics o lowering blood pressure...

Most physicians now agree on the importance of reducing blood pressure in the hypertensive patient. But high blood pressure exists, of course, only as part of a complete clinical picture. The hemodynamic profile of well-established essential hypertension is characterized by elevated arterial blood pressure, normal cardiac output, and increased total peripheral resistance.

And so, physicians are increasingly concerned with the effects of an antihypertensive agent not only on blood pressure itself but also on the hemodynamic pattern—in short, with the total effect of the drug. *Does* it indeed help lower blood pressure effectively? *Is* peripheral resistance reduced? *Are* cardiac output and renal functions maintained? And, also, is ther likely to be drug-induced pos tural hypotension seriou enough to pose a threat to th patient's cerebrovascula status?

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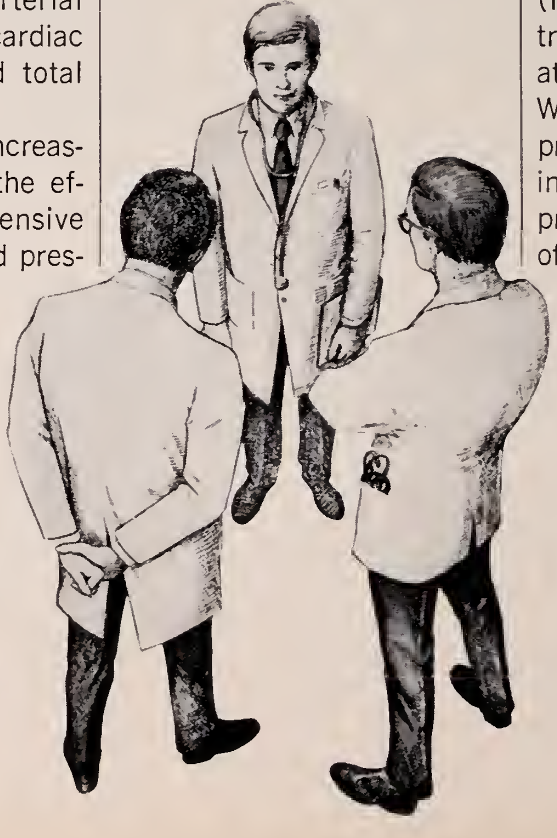
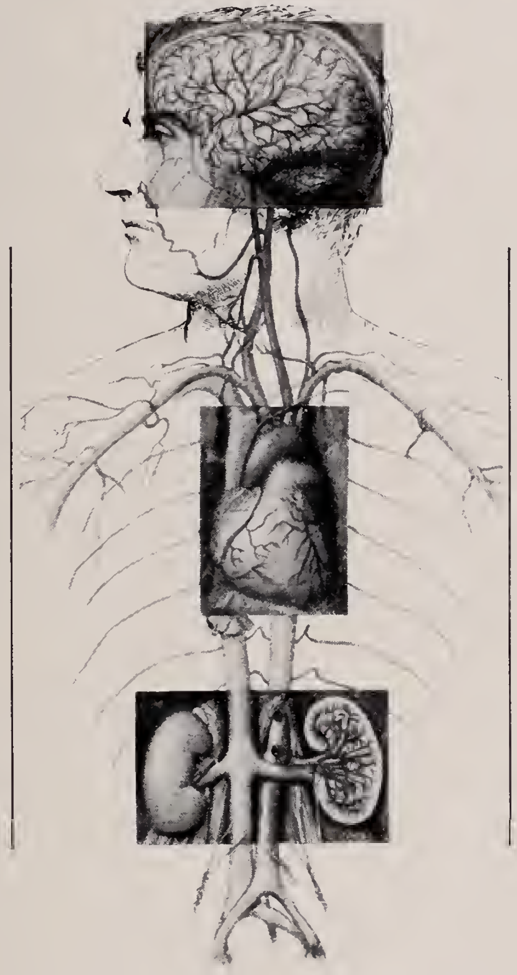
With its unique hemodynami profile, ALDOMET has draw increasing attention and ap proval from physicians. First, of course, for its efficacy i



the more physicians rely on this unique antihypertensive



ering blood pressure. But re are other considerations well. Cardiac output is usu- maintained with no cardiac eleration; in some patients heart rate is actually wed. Peripheral resistance apparently reduced. DOMET does not usually npromise existing renal ction; it generally does not uce renal blood flow, glo- rular filtration rate, or fil- ion fraction. And ALDOMET ally does not cause sympto- tic postural or exercise otension.

Contraindications include active hepatic disease and known sensitivity to the drug. Use with caution in patients with a history of liver disease or dysfunction. Not recommended in pheochromocytoma or pregnancy.

It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

In most cases of sustained moderate hypertension

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smoothly lowers blood pressure

a brief summary of prescribing information,
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500 mg TABLETS
as well as the standard
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In most cases of sustained moderate hypertension

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smoothly lowers blood pressure

Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis. Known sensitivity. Not recommended in pheochromocytoma. Unsuitable in mild or labile hypertension responsive to mild sedation or thiazide therapy. Use cautiously in patients with history of previous liver disease or dysfunction.

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between six and twelve months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at six and twelve months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first three weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first two to three months of therapy. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first six to twelve weeks of therapy or whenever an unexplained fever occurs. If fever, abnormalities in liver function tests, or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, reversible reduction in leukocyte count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur.

Use in Pregnancy and Childbearing Age—Not recommended in pregnancy. In women of childbearing age, weigh potential benefits against possible fetal hazards.

Precautions: Methyldopa may interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, spuriously high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has occurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: Sedation, usually transient, may be seen during initial therapy or when dosage is increased. Headache, asthenia, or weakness may be noted as early, transient symptoms. Symptoms associated with effective lowering of blood pressure are occasionally seen and include dizziness, lightheadedness, and symptoms of cerebrovascular insufficiency. Angina pectoris may be aggravated. Symptoms of orthostatic hypotension may occur; if symptoms occur, reduction of dosage is suggested. Bradycardia, nasal stuffiness, mild dryness of mouth, and gastrointestinal symptoms including distention, constipation, flatus, and diarrhea occur occasionally; these generally can be relieved by reducing dosage. Nausea and vomiting have been reported in only a few patients. Sore tongue or "black tongue," pancreatitis, and inflammation of salivary glands may occur.

Weight gain and edema occur infrequently and are relieved by administering a thiazide diuretic; if edema progresses or signs of pulmonary congestion appear, discontinue drug. A rise in BUN has been observed. Other rare reactions include breast enlargement, lactation, impotence, decreased libido, skin rash, mild arthralgia, myalgia, paresthesias, Bell's palsy, parkinsonism, psychic disturbances including nightmares, reversible mild psychoses or depression. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Note: Dosage should be limited initially to 500 mg daily when following previous antihypertensive agents other than thiazides. Maximal recommended daily dose is 3.0 g. Patients with impaired renal function may respond to smaller doses than patients with normal kidney function. Syncope in older patients has been related to increased sensitivity in those with advanced arteriosclerotic vascular disease; this may be avoided by lower doses. Tolerance occasionally seen either early or late, but more likely between second and third month after initiation of therapy; increased dosage or combined therapy with a thiazide frequently restores effective control.

How Supplied: Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

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(Continued from page 929)

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DECEMBER, 1974

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequ
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may be associated with temporary increase in frequency and/or severity o
seizures. Advise against simultaneous
gestion of alcohol and other CNS depr
sants. Withdrawal symptoms (similar
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occurred following abrupt discontinua
(convulsions, tremor, abdominal and
cle cramps, vomiting and sweating).
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According to her major
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patient with severe
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ngs, part of the problem
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ive anxiety, is often accom-
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e patient within a few
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For further information on this subject, the following references are provided:

1. Henry BW, *et al: Dis Nerv Syst 30*:675-679, Oct 1969.
2. Hollister LE, *et al: Arch Gen Psychiatry 24*:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics 11*:438-441, Sept-Oct 1970.

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tropics or anticonvulsants, consider
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Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

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President's Letter

The Gift of People

THIS IS THE SEASON of the year when our family seems to grow closer together, each more aware of the other's individual wishes, desires, and dedication. With this awareness there is an increased love and a wonderful joy in the season.

I hope that within the Minnesota State Medical Association the idea of being a family of physicians can become a reality. As in a family, each physician should act as an individual. But after open discussion without rancor, he should also commit himself to organized medicine's place in the welfare of the community.

It seems hardly proper for me to single out any one physician as an example of this commitment. Within my short period in the practice of medicine, there have been many physicians who have exemplified the scientific approach, concern for the individual, humility, compassion, intelligence, and sacrifice. Drs. Stickney, Swenson, McCarthy, Jacobson, Rice, Medelman, Buckley, and Campbell are just a few. These men, and others, are set apart as superior individuals. At the same time they have both promoted and honored the profession of medicine.

Reuben Berman is retiring as Editor with this issue of MINNESOTA MEDICINE. Dr. Berman is leaving behind three years of dedicated service. Within the confines of a limited budget, he produced a journal of excellence, a journal in which he, his editors, and his readers share pride. MINNESOTA MEDICINE, under his editorship has been a journal of and for the physicians of Minnesota, a forum where they could display their talents and abilities.

Mere words do not well describe this man. He is intelligent, scientific, compassionate, kind, and, above all, gentle. He often talks of "stepping on toes," but he walks so softly that one is always surprised to find he has stepped into the room. His diplomacy in dealing with people is unequaled. He is a sensitive man who never raises his voice, but is heard above others. He is firm in his convictions and in what he believes to be the truth.

Reuben to my mind exemplifies the complete physician and man. He believes in the goodness of all men, and his work has been predicated on that belief. He enriches the lives of those about him. It is a privilege to know and work with him. His continued presence on the Board of Editors will remind us in all seasons of the dedication, good humor, and intelligence in the medical family.

Bernard Hall M.D.
President
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Penicillium Species Fungus Growth on a Bionite Hydrophilic Contact Lens

IRVING SHAPIRO, M.D.*

Multiple Penicillium species fungus colonies are demonstrated to grow on a continuously worn Bionite hydrophilic contact lens without any apparent damage to the eye.

THERE IS MUCH CURRENT interest in the possibility of infections related to hydrophilic contact lenses. Bernstein,[1] in March, 1973, reported the first documented infiltration of a fungus, a yeast of the Rodotorula species, in a hydrophilic contact lens occurring under normal wearing, sterilization, and storage conditions. In an addendum to his report, two additional cases of fungus infiltration in a Bionite hydrophilic lens were noted but the type of fungus was not specified.

Bernstein after review of literature made the following comment: "During the course of the development of the newer H.E.M.A. Hydrophilic lenses, the manufacturers† as well as independent investigators‡ have conducted in vitro studies to determine whether fungus can grow within these lenses. Although various fungi were found to tenaciously cling to the lens surfaces despite the usual cleaning procedures, no fungal infiltration could be produced."

This report concerns the growth of grossly visible fungus colonies on the surface of a Bionite hydrophilic contact lens occurring while the lens was being worn.

Case Report

A 73-year-old woman presented November 1, 1973 with history of iridencleisis in 1939 and cataract removal in 1961, right eye. The left eye had iridencleisis in 1950, and currently contained a cataract. The corneas of both eyes were opaque. In the right eye there was iris and vitreous touch.

In February, 1972, a Bionite lens was placed on the right eye for continuous wear. This lens was replaced in June with a note having been made in her record that the previously placed lens had undergone some deterioration at its edge. It was further noted in the record that the lens was left in place continuously and that commercially available saline drops had been used topically with the lens in position on the eye.

On initial examination, multiple obvious whitish elevations were seen on the lens surface. In Figure 1 which shows the lens in position on the eye, one can see that the eye is white and nonirritated. The upper edge of the soft lens is visible in relationship to the filtering bleb. The white cornea can be seen through the lens. The portion of the lens lying over the upper cornea manifests multiple white elevations.

Figure 2 shows the lens removed from the eye and placed on a bluish-black background for better contrast. Again, multiple elevated whitish spots can be seen on the lens in its upper aspect.

The lens, after removal from the eye, was sent to the laboratory for microbiologic examination. The bacteriology report indicated that the whitish spots were a fungus of the Penicillium species.

Figure 3 shows the fungus colonies growing in appropriate medium.

Figure 4 shows the microphotographic characteristics of the fungus Penicillium.

After the lens was removed from the eye, the eye was left alone without medication. The eye did not appear clinically irritated in the presence of the lens and fungi and the eye remained quiet in appearance following the lens removal. A subsequent penetrating corneal transplant with anterior vitrectomy has been done and postoperative course to date has been good with good visual return and no suggestion of infection.

Comments

A study of 158 persons with no clinical evidence or recent history of ocular disease has shown fungi to be present on the lids or conjunctiva in 35 persons.[2] It is of interest that in one person showing a positive sampling for fungus that Penicillium species were found in this clin-

---

*Clinical Associate Professor, Department of Ophthalmology, University of Minnesota, Minneapolis, Minnesota.

†Soflens-Bausch and Lomb Company, Rochester, New York and Bionite Naturalens-Griffin Laboratories, Buffalo, New York.

‡Kaufman H. Dixon J., personal communication, 1970.

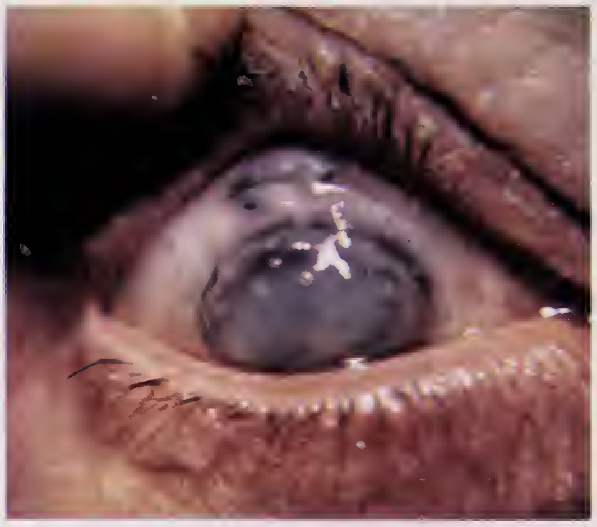

Fig. 1—Lens in position on the eye.

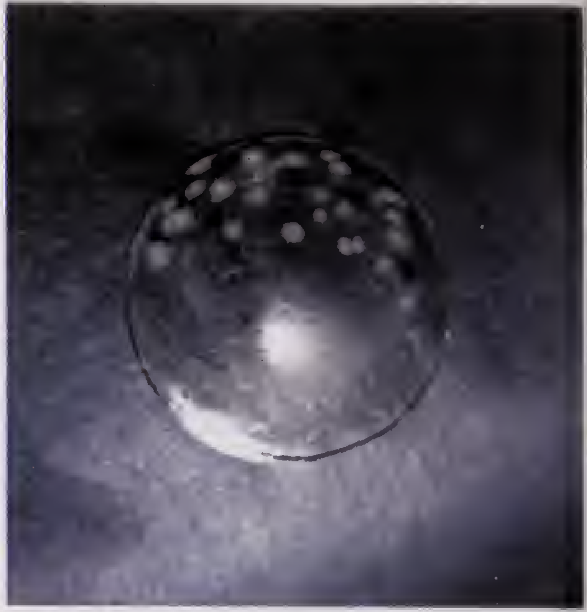

Fig. 2—Lens out of the eye.

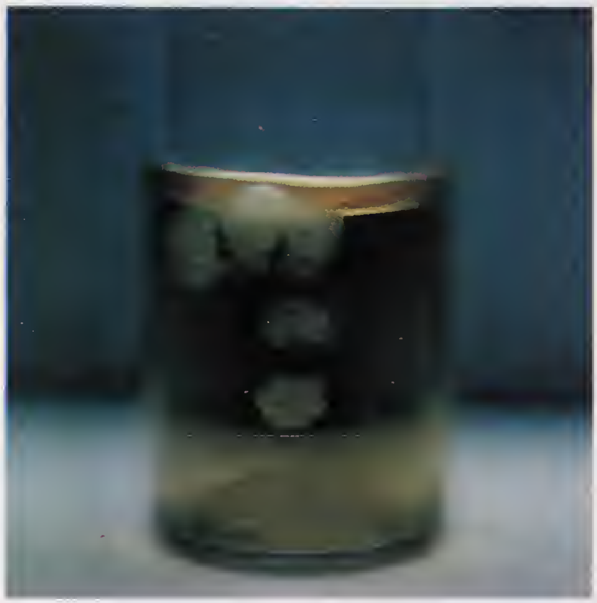

Fig.3—Fungus colonies growing in medium.

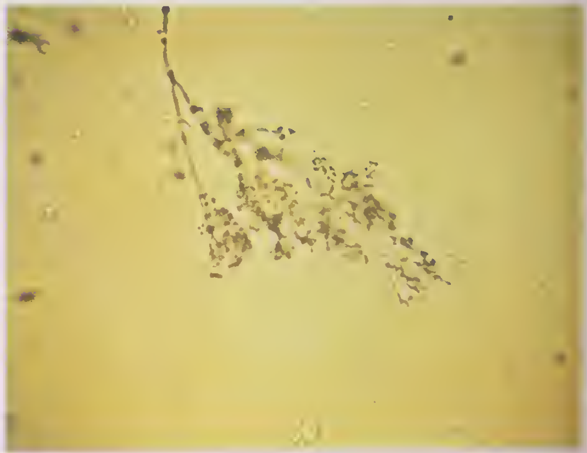

Fig. 4—Microphotograph of fungus Penicillium.

ically normal group.

This current report shows that a hydrophilic contact lens of the Bionite type when left in an eye for significant periods of time on a continuous wear basis, and treated topically only with saline drops, will allow growth of fungus colonies on the lens. It should be stressed that the lens was not removed and sterilized at intervals. It should be further emphasized that despite the presence of the fungi, no deleterious effect on the eye could be clinically attributed to the fungus.

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Folate Deficiency Due to Oral Contraceptives*

F. BRUCE LEWIS, M.D.†

A young lady with profound megaloblastic anemia and thrombocytopenia due to the use of oral contraceptives is described. Therapy with folic acid corrected the defect. Possible mechanisms are discussed.

MANY COMMONLY USED drugs are known to be capable of producing megaloblastic changes in the blood. Some of the more commonly used drugs include the anticonvulsant diphenylhydantoin (Dilantin), barbiturates, colchicine and numerous drugs used in cancer chemotherapy. The entire subject has been reviewed by Stebbins, Scott and Herbert.[1]

Recently a number of patients have been reported with megaloblastic anemia apparently associated with oral contraceptive agents.[2] Although the occurrence is undoubtedly extremely uncommon, one would expect that with the widespread use of these agents occasional cases will be encountered. This report is stimulated by the recent presentation of such a case.

Case Report

The patient, a 29-year-old unmarried female executive, was admitted to Midway Hospital because of a pounding pulse in the ears, easy bruising, fatigue and a sensation of weakness. Blood count the day previous had disclosed a hemoglobin of 6.8 Gms.%, a white count of 2,600 with 53% polys, many showing hypersegmentation and a platelet count noted to be decreased on smear. The patient had been in good health until early in 1973 when she had noted postprandial right upper quadrant pain. Workup led to a diagnosis of cholecystitis with cholelithiasis. A cholecystectomy was performed in June, 1973. At that time a hemoglobin of 10 Gms.% and a mean corpuscular volume of 110 was recorded. No further workup of the anemia was done. The patient was discharged on oral iron because of blood loss during surgery. Following her cholecystectomy, the patient noted alternating diarrhea and constipation and occasional gassiness. The remainder of the patient's history was not particularly significant.

Physical examination at the time of admission showed a pale but otherwise healthy appearing female who had scattered ecchymoses over all extremities. No lymphadenopathy was noted. Funduscopic examination disclosed two hemorrhages in the right fundus. Physical examination was otherwise unremarkable.

Admission laboratory evaluation at Midway Hospital disclosed a hemoglobin of 6.2 Gms.% with a MCV of 121, a MCH of 39.3 and a MCHC of 32.4. The platelet count was 77,000 and reticulocytes were 1.7%. The serum bilirubin was 0.8 mgs.% with a direct reacting fraction of 0.1 mgs.%. The lactate dehydrogenase was 4,170 units and the serum iron was 222 mcg/dl with a total iron binding capacity of 231 mcg/dl. A bone marrow aspiration was performed which disclosed typical megaloblastic changes.

The workup was originally directed towards ruling out pernicious anemia or malabsorption due to intestinal disease. A gastric aspiration was performed which disclosed normal hydrochloric acid secretion after stimulation with Histalog. A Schilling test showed 10% excretion of the radioactive B12, well within the normal range. Tests for intestinal function included fecal fat excretion which was 3 grams per day and a normal glucose tolerance test. A small bowel series was also normal.

It was noted at this time that the patient had been taking oral contraceptives (Ovral) for approximately three years. The contraceptive was stopped and the patient was started on oral folic acid. Serum B12 and folic acid levels had been drawn on admission and when returned two weeks later showed the B12 to be 180uug/ml (normal 150 to 600) and the folic acid to be 1.1 mug/ml (normal 5.3 to 17.0). On the fourth day of folate administration the patient's reticulocytes were 12% and they subsequently peaked at 24%. Her white count and platelet count promptly returned to normal levels and one week after the start of therapy her hemoglobin was 8.5 Gms.%. She was subsequently followed as an outpatient and on continued folate therapy her blood counts and morphology have normalized and the retinal hemorrhages have disappeared.

Discussion

An association between folic acid deficiency and the use of oral contraceptives has been increasingly noted.[2-4] Some reports have also appeared showing occasional decreases in serum B12 levels in patients on oral contraceptives both with and without folate deficiency but the majority of reports have demonstrated pure folate deficiency.[5] The possibility of co-existing intestinal disease has been considered in these patients and abnormal small intestinal biopsies have been occasionally noted.[6] The mechanism of action of the contraceptives on folic acid metabolism has been suggested to be inhibition of intestinal absorption of folate polyglutamate, the usual form of dietary folate. Therapeutic vitamin preparations which are monoglutamic folate are apparently well assimilated. Streiff[2] has shown that patients with folate deficiency and anemia could respond to small doses of monoglutamic folate while they previously did not respond to the polyglutamate in the diet.

---

*See editorial, page 967.

†St. Paul, Minnesota.

The patient reported here had apparently been on a normal diet containing adequate amounts of food folate but nonetheless developed severe malabsorption of folic acid.

If the postulated mechanism of action of oral contraceptives is correct, then it should be possible to administer these drugs to a patient such as this while concurrently maintaining adequate doses of monoglutamic folate. However, as pointed out by Herbert,[1] the suggestion of deficient intestinal deconjugation of polyglutamate folate induced by oral contraceptives is similar to the concept proposed for diphenylhydantoin induced malabsorption of folate. Recent evidence has cast some doubt on the latter mechanism and similarly the mechanism with oral contraceptives remains to be fully elucidated. Thus, it would appear prudent to recommend other forms of contraception in patients such as the one reported here or else observe such patients very carefully with frequent blood counts while oral contraceptives are administered.

It is unclear why this syndrome takes so long to develop although reports of other patients with the problem are similar. It would appear that at the time of the patient's surgery six months prior to her admission with severe anemia she was already moderately folate deficient in view of the hemoglobin of 10 Gms.% associated with a MCV of 110. One could postulate that the coexistence of a decreased postoperative dietary intake of folate plus the added stress on the marrow occasioned by surgically induced blood loss were the precipitating factors inducing the severe anemia noted on this occasion.

In view of what now appears to be a well established association between folic acid deficiency and the use of oral contraceptives in some patients periodic hemoglobin or hematocrit checks should be done on women who are using oral contraceptives. Even after administration of these agents for a substantial period of time without problem, there is still the risk of the insidious development of megaloblastic anemia. It would also seem wise to observe individuals on oral contraceptives particularly carefully after such stress as surgery, fad diets or other events which lead to decreased dietary intake of folate.

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A silent, dim, distanceless, steaming, rotting day in March . . . a soulless, skyless catarrhal day, as if that bustling dowager, old mother Earth—what with match-making in spring, and fêtes-champêtres in summer, and dinner-giving in autumn—was fairly worn out, and put to bed with the influenza, under wet blankets and the cold-water cure.*

---

*Charles Kingsley,Yeast, Chapter I. 1848.

Popliteal Aneurysms

LUIS H. TOLEDO-PEREYRA, M.D.[*] and YOSHIO SAKO, M.D.[*]

Eleven patients with popliteal aneurysms were studied at the Minneapolis VA Hospital in a period of seventeen years ending in 1972. Although there was a low incidence of popliteal aneurysms, our results suggest that the vein graft is superior to other forms of reconstruction. Primary end-to-end arterial anastomosis after aneurysm excision may also give an excellent result when this is technically feasible. In some patients, the relatively short period of survival suggests that clearly no surgery should be done in the face of severe disease elsewhere.

ONE OF THE conclusions drawn by Linton in his report on popliteal aneurysms 25 years ago[1] was that their incidence was increasing. Over a 17-year period ending in 1972, during which there were 176,196 hospital admissions, only 11 patients with popliteal aneurysms were seen on the Vascular Surgical Service of the Minneapolis VA Hospital. This seems incredible when considered in the light of hundreds[†] of operations performed annually on older men who need care for the treatment of abdominal aneurysms and for arterial occlusive disease. It has often been stated that if a popliteal aneurysm does not provoke any symptom, the aneurysm is apt to be overlooked until complications occur because only a cursory examination is apt to be made during a routine physical examination. Our records and recollection reveal not a single instance of popliteal aneurysm rupture, and although it is difficult to estimate how many instances of silent embolization or thrombosis have occurred, it has been rare that we have had to do an amputation because of complication occurring in a patient with an aneurysm that was undetected.

Trauma resulting from frequent bending of the artery has been described as a contributing cause to the development of a popliteal aneurysm. That trauma may play a role in developing an arterial aneurysm is suggested again by the recent observations of Abbott and Darling,[2] who reported the occurrence of eight axillary artery aneurysms in seven patients following chronic trauma from improperly used crutches. Generally however, degenerative changes secondary to arteriosclerosis must be the most significant cause as suggested by the histological examination of the aneurysms and by the frequent bilaterality of disease and association with other aneurysms. Almost half the patients in many reported series have bilateral popliteal aneurysms or have aneurysms located elsewhere.[3,4]

The treatment of popliteal aneurysms appears to have been one of the earliest problems in management of a vascular disorder and has been responsible for the development of various surgical procedures used in arterial surgery. These include such procedures as simple ligation, ligation and extirpation of the aneurysm with and without lumbar sympathectomy, excision and vein grafting as early as 1913, and angioplastic procedures on the aneurysm itself.[5,6]

The course of both surgically treated and untreated popliteal aneurysm is influenced by many factors. Through the years there have been a number of reports on the problem of popliteal aneurysm, but none can excel those from the Mayo Clinic for they span a period of 55 years describing their experience with operative and nonoperative management of 331 patients.[7-9]

The essential features of our 11 patients with popliteal aneurysms are listed in the Table. There were seven patients over the age of 70, the youngest was 50 years old. Four had bilateral popliteal aneurysms, one of these had in addition a femoral aneurysm and one both a femoral and an aortic aneurysm. In addition five patients had unilateral popliteal aneurysm only, one also had a femoral aneurysm and another one an abdominal aneurysm also. Despite the small number in our group, it resembles larger series in that there is a tendency to bilaterality and an association with aneurysms elsewhere.

---

[*] Department of Surgery, Veterans Administration Hospital and University of Minnesota, Minneapolis, Minnesota, 55417.

[†] E.g. 218 operations in 1972 and 235 operations in 1973.

Pain was the predominant symptom, it being reported by five of the 11 patients, three had no symptoms. Upon initial examination, all patients had pulsations in the aneurysm, one patient (No. 6) with bilateral popliteal aneurysms, had disappearance of the pulse on the right side in the interval between admission and operation. The aneurysm had thrombosed, but there was no loss of limb. Pedal pulses in the involved side were present in only seven of the 11 patients.

Angiograms were taken in only five patients, these being done in the latter part of the study. Generally a varying severity of occlusive disease was present. The advantage of having an angiogram is depicted in Figure 1. It shows division of the popliteal artery high in the popliteal space and showed that restoration of blood flow by grafting is feasible. One point that must be remembered is that the angiogram will usually no show the size of the aneurysm because of the tendency to form a clot leaving only a small channel through the aneurysm as shown in Figure 2 Failure to show an artery distal to the aneurysm does not necessarily preclude grafting because a recent embolus or thrombus may be causing the obstruction, thus probing and balloon-tipped catheter (Fogarty) passage should always be done after the aneurysm or artery is opened. One need only examine a few aneurysms to readily appreciate why thrombosis or embolus can occur and continue to be a major threat (Figure 3).

The results attained in our patients suggest that the vein graft bridging the defect after excision

TABLE
Popliteal Aneurysm 1955-1972 (11 Patients, all male)

Case No.	Age	Location and Size	Predominant symptom and Duration	Treatment	Follow-up
1.	62	L 3 cm	Claudication-five months	Saphenous vein graft & sympathectomy	Pulses present five ye, died of Ca of lung
2.	87	L 10 cm	Pain 12 months	Dacron graft	Pulse present six mon, died at home at 10 m hs
3.	52*	Bil. 4 cm	Pain lt leg six months	Lt below knee amputation, rt vein graft	Graft patient five year
4.	72†	Bil. 4 cm & 3 cm	None	No surgery.	Seen for six years, sev angina, legs unchange
5.	73†	R 4 cm	Pain three months	Above knee amputation on account multiple aneurysms and severe distal disease	Died five years later of coronary occlusion
6.	78	Bil. 4x7 cm & 3x3 cm	Pain rt three months, lt leg asymptomatic	Resection rt aneurysm, no reconstruction Lt vein graft, lumbar sympathectomy	Occlusion vein graft at ur months, died of myoca al infarction at six month
7.	71	L 3 cm	Paresthesia three months	Vein graft	Pulses present 15 mon, then patient lost to foll-up
8.	69‡	R 5.5 cm	None	Excision of aneurysm & end-to-end anastomosis	Died seven years p.o. (prostate, artery open
9.	84	L 5 cm	Pain, edema three months	Dacron graft	Died two months p.o. c myocardial infarct. Gra status unknown
10.	50	L & R 3 & 4 cm	Pain one year	Vein graft L & R in stages lt lumbar sympathectomy	Rt graft open three yea lt graft occluded in one year, claudication
11.	76	L 5 cm	None	No surgery	Died within one year of intra-abdominal Ca

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*Left common femoral artery aneurysm also and severe peripheral disease
†Abdominal aneurysm and femoral aneurysm also
‡Abdominal aneurysm also

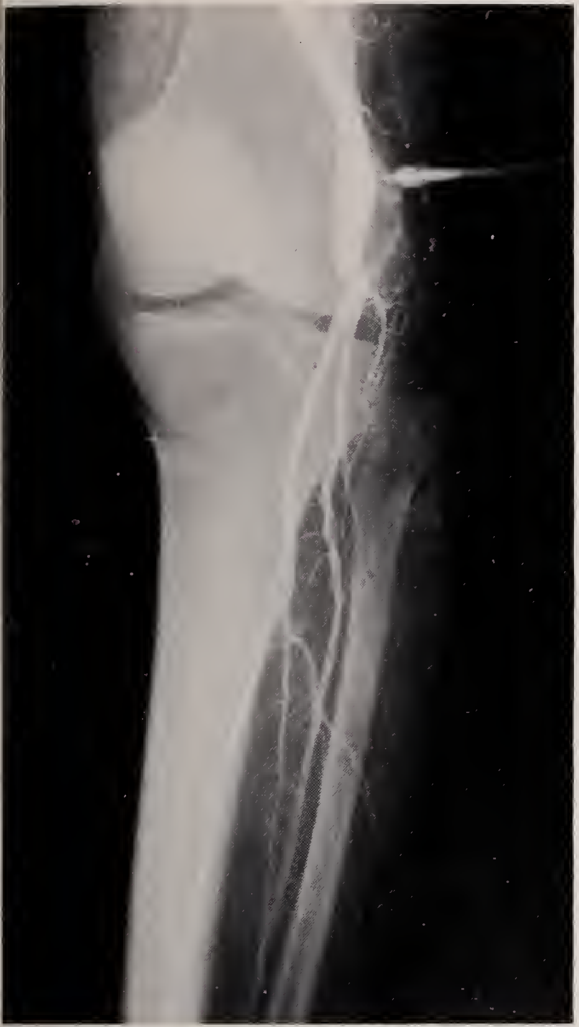

Fig. 1—Angiogram taken by direct injection into the aneurysm at operation; a procedure not generally recommended because of danger of embolization. The aneurysm was three times larger than what the Xrays showed. High origin of the tibial arteries is demonstrated.

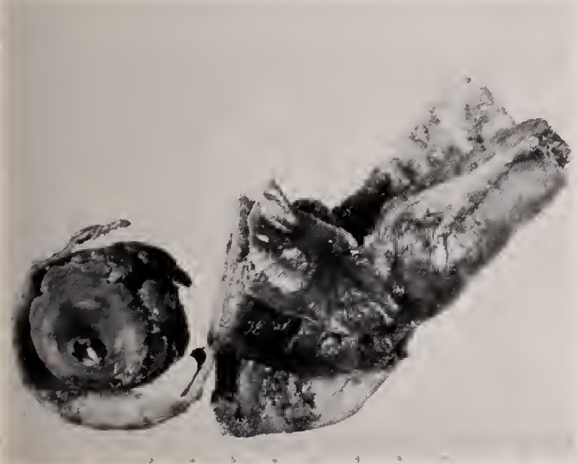

Fig. 2—Cross section of the aneurysm shows the usual situation of almost normal lumen with surrounding laminated clot.

of the aneurysm is superior to other forms of reconstruction (Patients 1, 3, 7, 10). Primary end-to-end arterial anastomosis after aneurysm excision may also give an excellent result when this is technically feasible (Patient 8). In other patients the relatively short period of survival suggests that clearly in some patients no surgery should be done in the face of severe disease elsewhere (Patients 2, 6, 9).

Discussion and Conclusion

In this era of modern vascular surgery, management of most popliteal aneurysms has become a relatively simple exercise in peripheral arterial surgery. Everyone agrees that a popliteal aneurysm represents a constant threat to the patient and should be surgically treated. The limitations of what can be accomplished depend upon whether the patient can tolerate any form of operation and the degree of the arterial disease in the leg. The procedure of choice is excision of the aneurysm and saphenous vein grafting. Vessel requirements for reconstruction are much the same as for treatment of occlusive disease. When acute

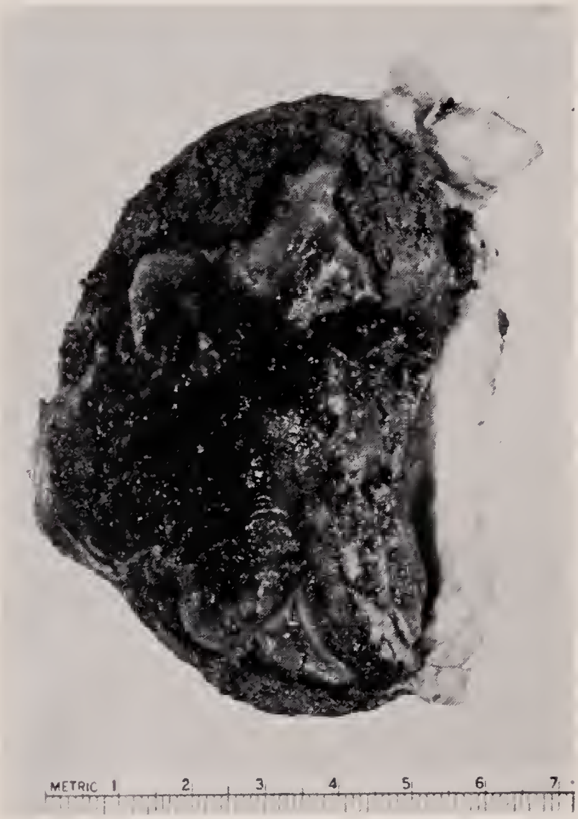

Fig. 3—Softening and liquefaction in a large aneurysm readily explains the high incidence of embolization and thrombosis occurring in a popliteal aneurysm.

ischemia is caused by thrombosis and/or embolization and operation is performed the main tributaries of the popliteal artery should be isolated and balloon-tipped catheter (Fogarty) be passed since the distal vessel may be opened and a bypass graft be performed.

In recent publications[9,10] advantages of bypassing the aneurysm have been mentioned. We have not tried this because we have found that a small aneurysm is readily removable and it appeared that a large one should not be left remaining (Figure 3) since infection may occur in it. We have used a modification of this in that the artery leading to and from the aneurysm is ligated as is done in the bypass procedure. The aneurysm is then opened and the clot is evacuated. The edges of most of the aneurysm wall are trimmed before a vein bypass is performed. This maneuver was chosen when continued dissection to free the aneurysm appeared to endanger the nerves and veins in the area because of obliteration of the usual plane of cleavage. When ligation and bypas is the procedure from the onset, two short incisions are made, one proximal to and one distal to the aneurysm and there is no dissection around the aneurysm. This maneuver undoubtedly lessens the risk of injury to nerves and veins in the poplitea space.

The place of lumbar sympathectomy in the management of popliteal aneurysm is unclear Our current thinking is that if a satisfactory vein replacement has been performed, the additional procedure of lumbar sympathectomy is not done whereas when every increment of increased flow to the leg is needed because of severity of the disease and there is no contraindication to extending the operation, the sympathectomy is done. In years past when ligation and excision was the treatment, a lumbar sympathectomy was also recommended.

We were impressed with the low incidence of the occurrence of popliteal aneurysms.

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At last there came a day when his system received a shock it was not destined to recover. This shock may best be described as a drama in three acts and two breakages:—

Act No. 1.—A careless servant breaks a valuable meerschaum pipe.

Act No. 2.—Careless servant carefully kicked down-stairs by General Donnerfels.

Act No. 3.—General Donnerfels breaks a blood-vessel.

The sequel to this drama was a threatening of haemorrhage to the lungs, rendered more alarming by the bitter cold which had just set in, for it was December.*

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*Jane Emily Gerard: His Uncle and Her Grandmother. Blackwood's Edinhurgh Magazine, 1890.

Recurrent Pheochromocytoma from Direct Peritoneal Implantation

Report of Two Patients with 22-Year Survival Periods

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WILLIAM H. ReMINE, M.D.* and SHELDON G. SHEPS, M.D.*

Recurrent pheochromocytoma developed in two patients following direct peritoneal implantation. In one patient, rupture of tumor occurred at the time of surgery; in the other patient, multiple small metastatic nodules were observed and removed surgically at the third operation. Both patients are currently still alive, but with disease, 22 years after treatment of the primary tumor. Long-term survival is compatible with this type of recurrent, metastatic pheochromocytoma, as the tumor is of low-grade malignancy.

Recurrence of pheochromocytoma from direct peritoneal implantation of tumor tissue does not appear to have been reported.[1] While reviewing the records of 138 patients with pheochromocytoma who were seen at the Mayo Clinic during the years 1926 through 1970 (unpublished data), we were able to retrieve the data of two such cases. These two cases serve to illustrate the observation that, though multiple tumors may recur from direct seeding, a shorter life span need not necessarily be the result of recurrence of tumor following direct peritoneal implantation.

Case Reports

Case 1

A 38-year-old woman, whose case was reported in detail in 1964 by Sheps and associates,[2] was first seen at the Mayo Clinic in 1951. At that time, she gave a three-year history of episodic headaches, weakness, hyperhidrosis, and air hunger. The episodes initially lasted for two to three minutes but gradually became more frequent and longer in duration. The result of the histamine provocative test was positive. The blood pressure was normal, and no other abnormality was found on physical examination. Results of other investigations, such as chest roentgenograms, serum corticosteroids, serum calcium, phosphates, electrolytes, hemoglobin, and urinalysis also were normal.

A tumor of the right adrenal gland was found at laparotomy. The tumor was reported to be about one-half as big as a golf ball, well encapsulated, and situated just above the right kidney. Manipulation of the tumor caused the patient's blood pressure to increase. During removal of the tumor, the capsule tore and some of the tumor escaped. The tumor looked necrotic; it appeared to be benign. Pathologic examination revealed several aggregates of tumor tissue (total tissue weight, approximately 55 g); microscopically, the diagnosis of a poorly encapsulated, low-grade pheochromocytoma was made. The patient was dismissed following an uneventful postoperative course.

Her symptoms recurred about eight years later. In 1961, symptoms similar to her original ones were associated with an increased blood pressure; on one occasion, following abdominal palpation, the blood pressure rose to 230/130 mm Hg. A second laparotomy revealed numerous metastatic implants on the capsule of the undersurface of the right lobe of the liver, in the retroperitoneal tissues of the right upper abdominal quadrant, on the surface of the upper pole of the right kidney, and on the gastrohepatic omentum; all visible metastatic tumors were excised. After the operation, the plasma catecholamine concentration was elevated and the result of the histamine test remained positive. The patient received two courses of radiation therapy.

In 1965, roentgenograms of the pelvis showed an osteolytic lesion involving the right ileum in the region of the right sacro-iliac joint. Between 1965 and 1972 the disease remained essentially unchanged. Catecholamine studies gave the following urinary excretion rates: vanillylmandelic acid, 3.4 to 4.6 mg/24 h (normal: <6.5 mg/24 h)[3]; metanephrines, 2.4 to 3.3 mg/24 h (normal: <1.3 mg/24 h); and catecholamines, 115 to 123 μg/24 h (normal: <338 μg/24 h). At the last examination in 1972, she had few symptoms and the

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blood pressure was normal: the urinary excretion of vanillylmandelic acid was 2.9 mg/24 h. that of the metanephrines was 1.6 mg/24 h. and that of the catecholamines, 162 μg/24 h.

Case 2

An 18-year-old woman, whose case was reported in detail in 1963 by Manning and associates,[4] presented at the Mayo Clinic in August 1951, with a five-year history of episodic palpitation with muscular weakness and frontal headaches, blurring of vision, and sustained hypertension (190/150 mm Hg). Chest roentgenograms and intravenous pyelograms and hemoglobin concentration were normal, as were the serum concentrations of 17-ketosteroids and corticoids, and the results of urinalysis. A Regitine test gave a positive result for pheochromocytoma.

At laparotomy, a lobulated tumor was discovered in each adrenal gland. Both tumors were removed, their capsules intact, but a small amount of adrenal tissue was preserved on each side. The tumor removed from the right adrenal gland weighed 35 g and that from the left gland, 55 g. The histologic diagnosis was that of bilateral multilobular pheochromocytoma. She was normotensive on dismissal.

The patient was seen again in August 1961, when she was hypertensive. Investigation confirmed recurrence of pheochromocytoma. Laparotomy revealed a recurrent tumor of the right adrenal gland. During palpation of the tumor the patient sustained cardiac arrest but resuscitation was successful. The tumor, which was adherent to the vertebral column and diaphragm, was removed together with a segment of diaphragm (6 x 4 cm). The specimen weighed 27 g; it consisted of multiple nodules of recurrent pheochromocytoma in the right adrenal gland, expanding the cortex, together with numerous other nodules of tumor (diameter, 1.5 to 3 cm) situated in the periadrenal connective tissue.

Because of persistent hypercalcemia (range of serum calcium 12.8 to 14.1 mg/dl) a presumptive diagnosis of primary hyperparathyroidism was made. The cervical region was explored one month after the second laparotomy. At operation, abnormal tissue from both the parathyroid glands and the thyroid gland was removed. The right inferior and left inferior parathyroid glands were excised, and part of the left superior parathyroid gland was biopsied; histologically, all of these glands showed chief-cell hyperplasia. In addition, because the right lobe of the thyroid gland was enlarged, a total right lobectomy and a left subtotal lobectomy of the thyroid were performed; the histologic diagnosis was grade 2 medullary carcinoma with amyloid stroma.

The patient was seen again on several occasions. In 1967, laboratory investigation showed that the urinary excretion of vanillylmandelic acid was 5.2 mg/24 h, that of metanephrines was 2.5 mg/24 h, and that of catecholamines was 768 μg/24 h. At that time, there was exacerbation of her hypertension, and biochemical investigations again gave evidence of recurrence of th tumor. At laparotomy, the liver was found to hav herniated through the diaphragm posteriorly and nu merous peritoneal implants were found in the righ upper quadrant; biopsy of the implants confirmed th diagnosis of recurrent pheochromocytoma. A large metastatic tumor was also found in the right lobe of th liver; during dissection for this tumor the patient sustained cardiac arrest, but she was again successfull resuscitated. She left the hospital on the seventh pos operative day; she was taking phenoxybenzamine (D benzyline).

The patient was seen again in July 1973, when sh had no symptoms except for occasional bouts of palpitation. Her blood pressure was 190/115 mm Hg (supine and 160/110 (sitting); at this time she was takin phenoxybenzamine (10 mg twice daily). Urinary excretion of metanephrines was 2.9 mg/24 h, that of vanillylmandelic acid was 11.1 mg/24 h, and that of urinar catecholamines, 172.3 μg/24 h. The serum calcium wa normal (9.3 mg/dl). She was instructed to take increasing amounts of phenoxybenzamine and propranolo hydrochloride (Inderal) to control the blood pressure and tachycardia, respectively.

The family history of this patient was interesting two other siblings were also afflicted with this triad o bilateral pheochromocytoma, medullary carcinoma o thyroid, and hyperparathyroidism.

Comment

In both of these patients, recurrence of pheochromocytoma was the result of direct seeding of tumor; in the case of the first patient, peritoneal implantation was the consequence of rupture of the tumor capsule during adrenalectomy. Experience with these patients further illustrates that a long period of survival is compatible with active, recurrent disease[5] and suggests that an attempt should always be made to remove as much of the tumor as possible. That both of these patients should be alive, with the disease still active, about 22 years after treatment of the primary tumor is of interest in view of the results of the review of records of patients with pheochromocytoma seen at the Mayo Clinic during the period 1926 through 1970: 13% of these patients' tumors were defined, on the basis of involvement of nonchromaffin tissues, as being malignant.[6] Reduction in bulk of tumor tissue present in the body facilitates management of the hypertension and alleviates the symptoms resulting from episodic release of epinephrine and norepinephrine into the bloodstream.

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3-6 Will be found on page 976.

Fluocinonide Cream

In A Variety of Dermatoses

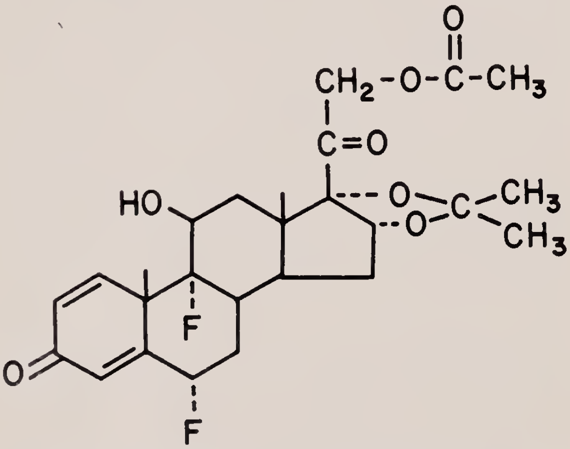
MANUEL O. JAFFE, M.D.* and THOMAS H. ALT, M.D.†

A double-blind trial of fluocinonide 0.05% in FAPG base versus hydrocortisone 0.5% was carried out for 14 days in 20 patients with various corticosteroid-responsive dermatoses. The drug preparations were applied unoccluded and assessed after two weeks.

Of the many different topical corticosteroids recently developed, fluocinonide—the fluorinated 21-acetate ester of fluocinolone acetonide (Figure)—has shown the greatest efficacy in both bioassay and clinical trials.

In a modification of the Stoughton-McKenzie vasoconstrictor assay, which correlates the degree of cutaneous vasoconstriction produced with the strength of the topical steroid applied, fluocinonide was found to have five times the potency of fluocinolone acetonide, triamcinolone acetonide, and betamethasone valerate when tested with normal human skin.[1] The results of a multicenter study involving 480 patients showed fluocinonide 0.05% was statistically superior to hydrocortisone 0.5% in psoriasis, atopic dermatitis, and lichen planus.[2] In another comparison between fluocinonide 0.05% and hydrocortisone 0.5%, the fluocinonide produced a statistically significant ($p<0.01$) clinical response in two groups of psoriatic patients.[3]

There is recent increase appreciation that the type of base in which a topical steroid is dispensed is equally as important as the actual strength of the steroid itself in the pure form. Burdick et al. convincingly demonstrated how an inappropriate base can prevent effective steroids from exerting their full potential.[4] An integrated steroid/base system is required for a balanced formulation that can effectively solubilize the drug and deliver it to the skin surface. Consequently, fluocinonide is dispensed in FAPG®‡ cream, a special vehicle that is a white semi-solid which combines the properties of a gel and a cream and consists of stearyl alcohol, polyethylene glycol 6000, propylene glycol, 1,2,6-hexanetriol and citric acid. A stable compound, it contains no added emulsifiers or preservatives—components that have caused sensitization problems with other topical preparations.[5,6] Early clinical trials in both double-blind and open assessments have demonstrated the therapeutic efficacy of fluocinonide 0.05% in the FAPG cream vehicle in a range of steroid-sensitive dermatoses.[7,8] A good therapeutic response has occurred in psoriasis without the necessity of occlusive dressings, in many cases in which treatment modalities have previously been tried and rejected.[9-10] To further test the usefulness of this drug, a double-blind trial of fluocinonide 0.05% in FAPG cream against hydrocortisone 0.5% was carried out in a selection of patients seen in private dermatological practice.



Figure—Molecular Structure of Fluocinonide (6α, 9α-difluoro-11β, 16α, 17α, 21-tetrahydroxypregna-1, 4-diene-3, 20-dione, cyclic 16, 17-acetal with acetone 21-acetate).

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Method

A group of 20 patients with bilateral and symmetrical lesions of psoriasis, atopic dermatitis, seborrhea, contact dermatitis, eczematous dermatitis, and lichen planus were assigned to the trial. Ages ranged from five to 76 years; 12 of the subjects were female, eight male. Duration of the skin ailments varied from several weeks to 23 years. Fourteen of the subjects had previously been treated with topical steroids, and five had previously received systemic steroids. Results had been poor to good. A 49-year-old man had concomitant diabetes mellitus; a 22-year-old woman was pregnant (two months); a 58-year-old woman was asthmatic; and a 76-year-old woman had arthritis, hypertension, and osteoporosis.

At an initial evaluation, the status of the lesions was assessed and all other topical drug therapy stopped. Each patient then received the test drugs in a set of identical tubes marked with an identification number and the letter "L" or "R" to denote which side of the body the cream should be applied. The two drugs were assigned to either side of the patient by a clinical monitor, using a set of randomized numbers; neither the physician nor the patients knew which tube contained which drug until the trial was completed. The patient was instructed to apply cream to the allocated side four times daily, without occlusion, and to massage the preparation in gently for a few moments.

The patients were assessed at 14 days, and lesion response to the medications was evaluated as positive (an improvement) or negative (no improvement or worse). Any complaints reported by the patients or problems observed by the physician were noted.

Results

Final assessment at 14 days included 19 patients. A six-year-old girl did not return for the last evaluation. The tabulation below shows that at 14 days 18 subjects improved with fluocinonide versus 11 with hydrocortisone.

Response	Fluocinonide	Hydrocortison
Positive	18	11
Negative	1	8
Total	19	19

Patient complaints with fluocinonide wer dryness (2), transient burning for a few second after application (2), and too greasy (2). Wit hydrocortisone, patients complained of stickines and irritation (1), burning and irritation (1), an redness (1).

Five patients were taking concomitant medication during the trial, but in no case was this considered to have influenced response with either fluocinonide or hydrocortisone. The diabetic patient was receiving tolazamide, a 23-year-old man was receiving diazepam, a six-year-old bo was receiving erythromycin, a 26-year-old woman was using an oral contraceptive, and the 76-year-old patient was receiving indomethacin and testosterone.

Discussion

In this small-scale trial of fluocinonide under double-blind conditions, the excellent results reported by other investigators seem confirmed. Of particular note were four patients who had suffered from psoriasis for many years and who had a moderate improvement after only one week's application of fluocinonide without occlusion. After the second week of the trial, fluocinonide produced a positive response in 18 of the 19 subjects evaluated, which indicates that fluocinonide is the more active preparation. Fluocinonide 0.05% in the FAPG base was well-received by the patients, with only a few complaints of dryness, momentary burning, or greasiness. The cream apparently gives the drug good release, without the need for occlusive dressings.

Summary

Final results show 18 patients having moderate to excellent improvement with fluocinonide versus 11 with hydrocortisone, adding further support to previous studies on the clinical efficacy of fluocinonide.

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Multiple Sclerosis

Recent Concepts of Etiology

THOMAS E. DAVIS, M.D.*

The etiology of Multiple Sclerosis remains unknown. A likely possibility is that a viral infection early in life somehow triggers production of a blocking antibody and sensitization of lymphocytes.

THE ETIOLOGY OF multiple sclerosis (MS) remains an enigma. It has puzzled investigators since 1835, when Cruveilhier first reported the characteristic changes of patchy "grey degeneration" in a spinal cord. Today MS remains a perplexing problem, a relentless disease inflicting all degrees of neurologic disability, particularly among young adults.

Etiologic Implications of Epidemiology

Clues to the etiology of multiple sclerosis have been sought through interpretations of its epidemiology; accordingly, many studies of prevalence, incidence, and mortality of multiple sclerosis in a wide variety of countries have been reported.

There is some evidence that susceptibility is genetically determined. Between five and 10 percent of sufferers have relatives with multiple sclerosis.[1] The concordance rate for monozygotic and dizygotic twins is 20%, for siblings it is 6.5%, for parents 1.7%, and for cousins 0.4%, compared with an expected rate of 0.05% in the general population.[2]

It has long been evident that multiple sclerosis is more common in temperate countries than in the tropics, that progressively higher incidence and prevalence rates at latitudes farther from the equator are present in Europe, North America, and Australia.[3] In Japan and in South Africa, multiple sclerosis is allegedly rare both in northern communities and in southern regions. In addition, foci of extremely high incidence have been demonstrated; such are known to exist in Switzerland, in some Scandinavian countries, as well as the Orkney-Shetland Islands.[4]

Detailed study of the incidence and prevalence of multiple sclerosis among immigrant groups, from areas of low risk, have provided illuminating results. Dean reported the prevalence of MS among immigrants to the Republic of South Africa who migrated from Britain and other parts of northern and central Europe was about forty-nine per 100,000 population. In comparison, the native born white South Africans have prevalence rates of about eleven per 100,000 for the English-speaking, and three per 100,000 for the Afrikaans-speaking groups.[5] Alter et al[6] studied Israeli immigrants and native-born Jewish populations, and noted that the disease is rare among immigrants from other Near East countries and North Africa, but it is considerably more frequent among immigrants from Central Europe, and even higher among those from Northern Europe. Alter et al.[7] confirmed these findings in a study of the prevalence of MS among native-born and immigrant populations of Hawaii. It was found that the prevalence rate of the disease among various immigrant groups reflects that of the area of origin of the immigrant. Further study of the data revealed that age of immigration appears to play an important role, since a person leaving his country of origin roughly before the age of 15 would have the risk of acquiring MS similar to that of the new place of residence; an individual immigrating after that age would carry with him the risk factor of his country of origin. According to these studies, the age of 15 would appear to be a "critical" one in regard to the acquisition of MS.[8]

Leibowitz et al.[9] reported that better sanitation in the childhood home (on or about age 10) was reported by significantly more patients with MS than by matched controls. This suggests the possibility that in subjects who develop MS there is a lesser contact with a potential agent during early life with failure to develop protective immunity and greater susceptibility to it later in childhood or adolescence.

Infective Hypothesis

At the present time, the most strongly considered etiologic factor in multiple sclerosis is infection, as an increasing body of evidence supports the long suspected role of virus infection as a cause of multiple sclerosis.[10-17] In 1962, Adams and Imagawa[16] reported slightly higher serologic titers to measles virus in multiple sclerosis than in control subjects. However, subsequent studies of the relationships of multiple sclerosis to measles infection have not shown such a connection. Higher titers of measles antibody in the CSF have not been found consistently and some studies have not found significant differences between multiple sclerosis subjects and controls. Brody et al.[15] summarized such studies. He found that virus antibody titers of MS patients were higher than titers of carefully matched controls not only for measles, but for type C influenza, herpes simplex, parainfluenza 3, mumps, and varicella-zoster as well. Virus antibody titers among MS patients were not higher for any of these agents than were titers of the siblings of the same sex born within three years of the patient, suggesting a possible shared environmental factor to account for these responses.

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Poskanger et al. have shown a similarity between some epidemiologic characteristics of MS and those of poliomyelitis, which affects individuals who have not developed immunity from an infection in childhood. In areas where hygienic standards are poor, poliomyelitis is usually a benign disease of infancy, and in these areas the risk of MS also has been found to be low.[18] The incidence of both diseases correlates reasonably well with the general level of sanitation. These observations have led to the hypothesis that MS is the result of an infection with an unknown agent which produces severe effects in adults who were not immunized in childhood by contact with the infective agent.

While some of these epidemiologic studies may give credence to the idea of a viral infection with a long latent period, there appears to be little similarity between the usual long, intermittent course of multiple sclerosis and the subacute, relentlessly downhill course of proved slow viral infections such as kuru, Jakob-Creutzfeldt disease, progressive multifocal leukoencephalopathy, and subacute sclerosing panencephalitis.[19] Slow virus culture techniques in MS patients have not met with success.[1] Nevertheless, it is being suggested that MS might be considered as the chronic form of reaction of the nervous system to the measles virus, as subacute sclerosing panencephalitis has now been shown to be the subacute form.[19]

A specific viral agent as the cause of MS has not been found. At the present time, epidemiologic studies are pointing strongly to the possibility that MS may be acquired in childhood, and it is now being suggested that an infection during the first 15 years of life could induce hypersensitivity to either the infective agent or an autogenous antigen. When released by subsequent infections, this component could provoke an autoimmune reaction at the site of its release, causing demyelination.[20]

Autoimmunity

The epidemiologic data with its emphasis upon environmental factors, while supporting the idea of an infectious etiology, in no way militate against the other prevalent theory of etiology, i.e. that of an autoimmune or allergic reaction of the nervous system. The demonstration of high levels of IgG in the cerebrospinal fluid, and subsequently of equally high levels in brain tissue, provides support for this hypothesis.[19] The evidence for a specific immunological disorder in MS is not definite because the presence of immunoglobulins could be the cause of the disease or could be a response to an infective agent. Complement-fixing reactions to various brain constituents have been reported in patients with MS, but these reactions appear to be non-specific, as they also occur in patients with other CNS diseases.[21]

Bearing on the possible immunologic pathogenesis of multiple sclerosis have been the extensive investigations of experimental allergic encephalomyelitis (EAE), the model autoimmune disease with strong resemblances to human acute disseminated encephalomyelitis, which has for many years been considered indistinguishable from multiple sclerosis in its acute form. EAE is produced by intradermal injection of a protein component of central nervous system myelin. Ultrastructural studies of EAE have revealed an orderly sequence of cellular events leading to a destruction and removal of myelin with sparing of axons (primary demyelination). Sera from animals with EAE and humans with acute MS rapidly produce a reversible block of complex electrical activity when applied to CNS tissue cultures, which suggests a possible mechanism for transient symptoms in MS.[22] This so-called myelinolytic factor found in serum of MS patients and animals with EAE appears to be a complement-dependent antibody. Nonetheless, the level of circulating myelinolytic factor is increased in other diseases of the central nervous system, so it cannot be regarded as a specific feature of multiple sclerosis.[21]

The possibility of a viral factor and the possibility that immunological mechanisms play a prominent role in the pathogenesis of MS are not then mutually exclusive. Unlike the animal model, EAE, and unlike human postvaccinial encephalomyelitis, both of which are produced by intradermal injection of CNS tissue, no such direct exposure to an antigenic agent is known to exist in MS. If MS is an immunological disease, some triggering event is required to set the immunopathogenetic mechanism in motion. A viral infection of the CNS could conceivably play such a triggering role by causing a breakdown of some myelin, with resultant release of encephalitogenic proteins or peptides. The response to the presence of the released encephalitogen might be the production of a functional blocking antibody and the sensitization of lymphocytes. The former might be responsible for acute, transient deficit phenomena, while the consequence of the latter would be a cell-mediated demyelinative reaction, with the combination of these factors ultimately producing the clinical picture of MS.

Vascular Factors

The fact that plaques of multiple sclerosis appear to be centered around small veins and venules has led to the observation that many of these vessels contain thrombotic occlusions. However, further observance has shown the occlusions to be the result, rather than the cause of the lesions.[21] Other investigations into possible vascular factors now reveal that adhesiveness of platelets is increased in multiple sclerosis and that the fibrinolytic activity of the blood is elevated.[23] Again, it is not known whether these changes are an antecedent to venous thrombosis and at the present time, there is no convincing case that venular thrombosis plays a pathogenic role in the disease.

Metabolic Factors

The possibility that MS might be due to a deficiency in essential fatty acids has been considered. One group noted a deficiency of trienoic fatty acids in the white matter of a case of MS,[21] while another group found a deficiency of unsaturated fatty acids in the lecinthins from similar material, and reduced linoleic acid in plasma from patients with the disease.[21] These fatty acid changes could be the result of the disease, rather than the cause.

Conclusions

1. Susceptibility may be genetically determined.
2. MS is usually more common in latitudes further from the equator.
3. Prevalence rates among immigrants reflect that of the area of origin of the immigrant.
4. The age of 15 seems to be a critical one for the acquisition of MS.
5. It is associated with higher levels of environmental sanitation.
6. MS patients have had higher serologic titers to measles virus, as well as several other viral agents.
7. There is little clinical resemblance between MS and the so-called slow virus infections.
8. MS resembles to some extent experimental allergic encephalitis.
9. An infection during the first 15 years of life could induce hypersensitivity to either the infective agent or an autogenous antigen.
10. A viral agent might trigger the release of some encephalitogenic protein or peptide by causing a breakdown of myelin. This encephalitogen might cause production of a blocking antibody and the sensitization of lymphocytes—the former causing acute deficit phenomena, the latter causing a cell-mediated demyelinative reaction.
11. There would appear to be no convincing evidence that vascular factors play a role in pathogenesis of MS.
12. The significance of abnormal essential fatty acids in MS patients is unknown at this time.

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12-23. Will be found on page 976.

Blindness

A Complication of the Repair of a Fracture of the Floor of the Orbit

W. J. SLACK, M.D.*

Complications from surgical repair of fractures of the orbital floor have recently been more recognized. These complications should lend direction in determining the primary course of therapy in treating newly discovered blow-out fractures of the floor of the orbit.

FRACTURE OF THE FLOOR of the orbit was first described in 1889; the clinical picture has been described by many authors since then. The need of early recognition and treatment of this condition is now well known. Although treatment may vary, basically the fracture is repaired through a transpalpebral approach or via the maxillary antrum. The fracture of the orbital floor may be the only injury sustained, but it usually is associated with other facial trauma and multiple facial bone fractures. Milaukas,[1] in his series of 84 patients with a fracture of the floor of the orbit, found 14% with ocular complications such as rupture of the globe, vitreous hemorrhage, hyphema, glaucoma, and angle recession.

Few authors have reported *ocular complications following treatment of a fracture of the floor of the orbit*—until Nicholson's[2] report in 1971. In reviewing 72 cases of fracture of the floor of the orbit, Nicholson found six in which the vision was lost, possibly as a result of the surgical repair procedures. It is notable that his extensive review of the literature disclosed only two cases, other than his own, in which this complication has occurred.

Case History

A 17-year-old male was admitted on August 7, 1972, to a local hospital for repair of a previously diagnosed fracture of the right mandible sustained in a fight in August of 1972. Other than an extremely sore jaw, he had no complaints. Physical examination revealed a tenderness at the angle of the right mandible, limitation of jaw opening, and a mild ecchymosis and swelling of the left upper lid and lower lid. Ophthalmologic examination showed 20/20 visual acuity bilaterally with no diplopia, enophthalmus, or exophthalmus. There was no extraocular muscle imbalance. Mild anesthesia was present over the distribution of the left infraorbital nerve. Lid ecchymosis precluded digital palpation to ascertain the possible presence of the step-fracture deformity of the orbital rim fracture. A 360 degree mild subconjunctival hemorrhage was apparent. The globe appeared to be freely floating and moving in a "full" but not tense orbit. The interpalpebral fissure was adequate for examination of the normal orbital contents.

Initial Xrays confirmed the fracture of the right mandible. The left maxillary antrum was opacified presumably due to blood in the sinuses. There was a fracture involving the anterior wall of the left maxillary antrum with no significant displacement. Planography showed the fracture of the orbital rim on the left with the lateral portion of the floor being minimally displaced downward.

Preoperatively the patient was given 1 gm/day of penicillin G. On August 8, 1972, under nitrous oxide and Fluothane anesthesia, interdental wiring was done to stabilize the fractured mandible and investigation of the fracture of the floor of the left orbit and the orbital rim was carried out through a transpalpebral approach. The fracture of the floor was identified and a Caldwell-Luc antrostomy was performed so that a two fold approach could be accomplished. This was a standard approach for this problem for this plastic surgeon. A rather "small size" Teflon implant was placed subperiosterally on the orbital floor and the maxillary antrum was packed with gauze. The whole procedure took an hour and 25 minutes.

Postoperatively the 1gm/day penicillin was continued. An initial dosage of 1.2 million units of Bicillin had been given intramuscularly. Mild analgesics were given for relief of pain and the usual postoperative care for the patient was established. On the evening of the day of operation, the patient had one small emesis. Subsequent to that he had no other problems on that day.

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The nurses observed that the eye pad was "in place and dry."

On the *first postoperative day*, the patient had minimal eye discomfort but experienced significant jaw and tooth tenderness requiring repeated and regular use of analgesics. Again the nurses noted that the left eye dressings were intact and dry.

On the *second postoperative day*, the jaw pain persisted. At this time, the nurses reported the eyelids were swollen closed and were tense. Lid edema precluded visualization of the globe.

On the *third postoperative day*, the orbit was still grossly swollen; dressings were dry and intact. The antrostomy pack was removed in the morning and the "pain" diminished shortly thereafter. The evening nursing notes revealed that the lid swelling had decreased but now the patient complained that he had some trouble seeing from the left eye. On the *fourth postoperative day*, the visual status of the left eye was confirmed to be decreased at that time. Immediate eye consultation was requested and the ophthalmologist's funduscopic examination disclosed a typical central retinal artery occlusion. There was proptosis of 6-8 mm, moderate lid ecchymosis and edema, as well as absence of a direct pupillary reaction to light in the left eye. Only a partial indirect response was noted. A partial left ophthalmoplegia was evident with the eye moving only to the midline laterally and decreased in all fields of gaze. The intraocular pressure was normal.

Immediate orbital decompression was advised and, in addition, Mannitol was administered intravenously in an attempt to reduce intraorbital pressures and try to re-establish central retinal artery blood flow. Within two hours after the consultation, the plastic surgeon and the ophthalmologist had removed the Teflon implant via the original transpalpebral route. Beneath the implant was a small, organized clot which appeared to occupy only a minimal amount of space. The implant was very small and had been well placed over the fracture site. There was no evidence that it had migrated posteriorly or had caused ecchymotic or traumatic areas either to periorbita or to the bony structure of the orbit. At this time, the left eye was proptosed in a straight forward line. Forced duction testing surgery showed moderate restriction of the globe excursions. Funduscopy immediately after extraction of the stent showed no evidence of vascular change. Seven hours after that, the patient said that his left eye felt better and examination showed that the indirect pupillary responses were starting to return and his ophthalmoplegia was decreasing.

The patient was discharged on his *fifth postoperative day* with a normal indirect pupillary response, still no direct pupillary response, but with a return to normal of the extraocular muscle movements. He had no light perception with the left eye.

Discussion

Nicholson and Guzak divided their cases into two categories.[2] In the first category, early loss of vision was associated with optic nerve injury. The second category, delayed visual loss, was associated with an increase in intraorbital pressure. Our case most closely resembles the fourth case illustrated in Nicholson's report with loss of vision, ophthalmoplegia, proptosis, lid swelling, orbital chemosis, and a fundus picture of central retinal artery occlusion. The exact cause of the orbital edema cannot be pinpointed, but I feel was probably a combination of intraorbital hemorrhage and conjunctival chemosis. I saw little evidence of retrobulbar hemorrhage but the chemosis was evident. The problem was one of increasing pressure from whatever cause is a closed space.[3,4]

The problem is *not* found in treating the *obvious* fracture of the floor with *obvious* diplopia or increasing diplopia or with enophthalmus. *The problem* is what one should do with the *isolated fracture* with minimal displacement, diagnosed by Xray, and dubious clinical manifestations. Two schools of thought prevail. One advocates investigation and repairing all floor fractures, while the other advised investigating only those with diplopia or enophthalmus of clinical significance and *especially* if *increasing* in degree of severity.

Whereas a mandatory "look" is advocated by some, our experience in this case points up the not commonly realized possibility that surgical intervention could lead to disaster. The isolated, and clinically asymptomatic fracture of the floor of the orbit probably should be left alone and treated conservatively with regular follow-up. If surgical intervention is necessary, meticulous and careful tissue handling is particularly important in an attempt to decrease the tissue edema and to prevent occurrence of intraorbital hemorrhage.

Experience additionally dictates that in postoperative follow-up, one must monitor very closely the visual status, the pupillary function, and the retinal status.[3] Pain appearing postoperatively is an absolute indication for investigation immediately. There is a distinct possibility that the pain exhibited by this patient was greater from the jaw than it was from the eye—thereby masking the importance of his ocular pain. It is essential that one localize the complaint of pain to its specific origin.

If possible the postoperative eye dressing should be omitted. If any at all is used, it should be a light one, although Nicholson is of the opinion that tight eye dressings are not a problem. More important the patient should not lie on the operated eye, since pressure so produced can lead to a prolonged, increased intraorbital pressure and ischemia.[5]

As ophthalmologists, we treat only a small fraction of the fractures of the floor of the orbit. Most of these fractures are associated with facial trauma and as such are seen and treated by the plastic surgeons and otolaryngologists.

We do see most of the patients in consultation. Here lies our opportunity to improve the care of such patients. Once we know that a surgical procedure is contemplated, we should make a special effort to follow the ocular status. Accepting a more relaxed and casual attitude during the postoperative course might lead to an ocula disaster.

Of primary importance is the recognition b all the physicians treating fractures of the floo of the orbit that ocular *complications* can occu with the repair of the isolated fracture of th floor of the orbit. Therapy in these fractures can best be carried out by combined approach involving the specialties of plastic surgery, otolaryngology, and ophthalmology, with all being involved

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Minnesota Academy of Ophthalmology and Oto-Laryngology Meeting

December 13, 1974—University of Minnesota, Nolte Center
Speaker: Theodore Schlaegel, M.D., Professor—Indiana Medical Center
Topic: Recent Advances in Uveitis and Histo Plasmic Choroiditis
Contact: James Sager, 227-8808.

Covert Drug Abuse

Among Young Hospitalized Psychiatric Patients

STEPHEN C. BUTZER, M.D.* and DAVID W. CLINE, M.D.*

A series of fifty psychiatric inpatients, ages 15-25 years, were studied regarding their use of drugs illicitly from one to nine weeks. 14.4 percent of 153 urine samples were positive for barbiturates and/or amphetamines and 78 percent of the patients had used drugs before entering the hospital. A lower incidence of illicit drug use in hospitalized patients is related to the unit's therapeutic community program.

DRUG ABUSE BY psychiatric inpatients has received increased attention, not only because of the obvious roadblock to efficacious therapy it represents, but also because clinical reactions to illicit drug use are many and varied. Indeed illicit psychotropic drug use and its undesired sequelae might be termed the "new great imitator" of traditional psychiatric syndromes. There have been several publications reporting high incidence of illicit use of psychoactive compounds by young psychiatric inpatients.[1,2] Another report showed that, prior to psychiatric hospitalization, use of illicit chemicals is the norm rather than the exception among the 15 to 25-year-old patient group.[3] We think, that although the studies showing the frequency of illicit drug use by psychiatric patients before hospitalization were accurate, that the statistics showing incidence of inpatient illicit drug use were not universally applicable. Specifically the degree of drug abuse by inpatients might be highly correlated to the type of psychiatric unit and the theoretical framework under which it operates. For instance, a unit that was community-oriented with peer pressure and a multiple feedback system where individual responsibility was emphasized would have significantly less drug abuse than in the traditional unit emphasizing the primary therapist-patient interaction.

Following the protocol of Blumberg et al.[2] we determined the incidence of illicit drug use on the Adolescent Young Adult Psychiatric Service of the University of Minnesota Hospitals. This unit is a 20-bed inpatient service for psychiatric patients in the age range of 15-25 years. Its theoretical structure and operation is based on the therapeutic community with an open system including multiple feedback mechanisms. Pathological behavior of community members becomes "public property" and is examined in a seven day a week community meeting, twice weekly small group therapy session, task groups supervised by Occupational Therapists, bi-weekly psychodrama-role-playing, and family therapy conferences. Group therapy and drug therapy (major tranquilizers and anti-depressants only) comprise the unit's treatment program and the staff role modeling manifests strong sanctions against illicit drug use. Although there were no prescribed punitive measures for illicit drug use, there was the strong operational expectation that the patients would not be involved in such activity.

Fifty consecutive admissions to this unit were included in this study. This group's age range was between 15 and 25 with a mean of 18.6 years. Diagnostically, thirty patients (60%) were classified as having a major psychosis which included manic-depressive illness, toxic psychosis, or the schizophrenias. Nineteen (38%) received a primary diagnosis in the non-psychotic category, which were usually adjustment reactions, but also included neurosis and personality disorder. One patient (2%) had a diagnosis of organic brain syndrome, secondary to cerebral palsy.

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Reprint requests to Mayo Box 393, 412 Union Street, Southeast, Minneapolis, Minnesota 55455 (Dr. Butzer).

These patients were followed with random urine samples obtained usually on Monday mornings without prior announcement. All results were withheld from anyone connected with the unit until after completion of the study. The urines were analyzed for presence of illicit drugs by methods that are standardized and described in other publications.[4,5]

Results

Histories taken from these patients on admission revealed that they had used drugs extensively before hospitalization. Like the group studied by Shearn and Fitzgibbons,[3] our group followed the "norm" of psychiatric patients in other areas of the country in the use of mind altering chemicals before coming to professional care. Ten percent had tried opiates, but none became dependent. Twenty-eight percent had used amphetamines, usually in conjunction with "downer" type drugs, as reflected by the thirty percent that used barbiturates. Forty-two percent had used hard hallucinogens, such as LSD, psilocybin, "STP," "PCP," and mescaline. Seventy-two percent admitted to significant use of marihuana and other cannabis derivatives and seventy-eight percent abused alcohol. Abuse of alcohol refers to the patient admitting to be subjectively intoxicated so that his judgment was impaired and/or the alcohol use resulted in antisocial behavior or involvement with the legal system.

TABLE 1

Drug Use Before Hospitalization

Type	%
Opiates	10
Barbiturates	30
Amphetamines	28
Hallucinogens	42
Marihuana	72
Alcohol	78

Like Blumberg, we did not get 100% of our patients to provide urine samples, but we did get eighty-six percent return of samples sufficient enough in volume to analyze (153 out of a possible 171). The number of consecutive samples per patient varied from one to nine. Twenty-two of 153 samples contained illicit drugs (14.4%): 9.8 percent of urines were barbiturate positive and 5.2 percent were amphetamine positive. One sample contained drugs of both classifications No opiates were found. It is presently not possible to detect cannabinoids or hallucinogens in urine samples and although occasional use was suspected on the unit it was felt to be sporadic.

TABLE 2

Comparison of Two Studies of Inpatient Illicit Drug Use

	Blumberg et al.	Presen Study
Total % of urines positive for drugs	60.0%	14.4%
Barbiturates	53.0%	9.8%
Amphetamines	24.1%	5.2%
Opiates	12.6%	0.0%
% of possible samples collected	84.0%	86.0%
Number of Patients	332	50

Discussion

These results were consistent with our expectation that there was less illicit drug use on this unit (14.4%) compared with the unit studied by Blumberg (60%). We suggest that the major reason for this difference relates to the nature of the inpatient programs. This program is based on a general systems approach which uses the therapeutic community as an operational working system. Each member has carefully selected or manipulated each other member of the system, adjusting his or her own behavior so that there is a complementarity of relationships, responding to individual needs, strengths, cultural values, and psychopathology. The purpose of such manipulation is to get the system to function *as a system,* maintaining solidarity of the community and insuring that members of the system work together in an effective program. Manipulations of community members occur through various group activities which focus on the primary task of studying individual patients in group behavior. Individual problems become group problems and conformity, which is an important issue for this age group, modifies previous group norms regarding the use of illicit drugs. The therapeutic community appears to be influential in decreasing the covert use of illicit drugs by young psychiatric inpatients.

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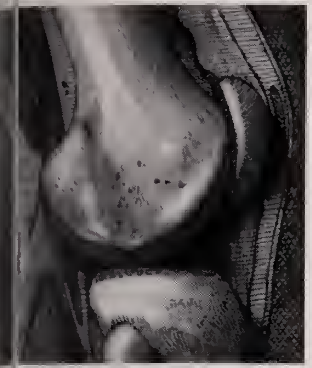

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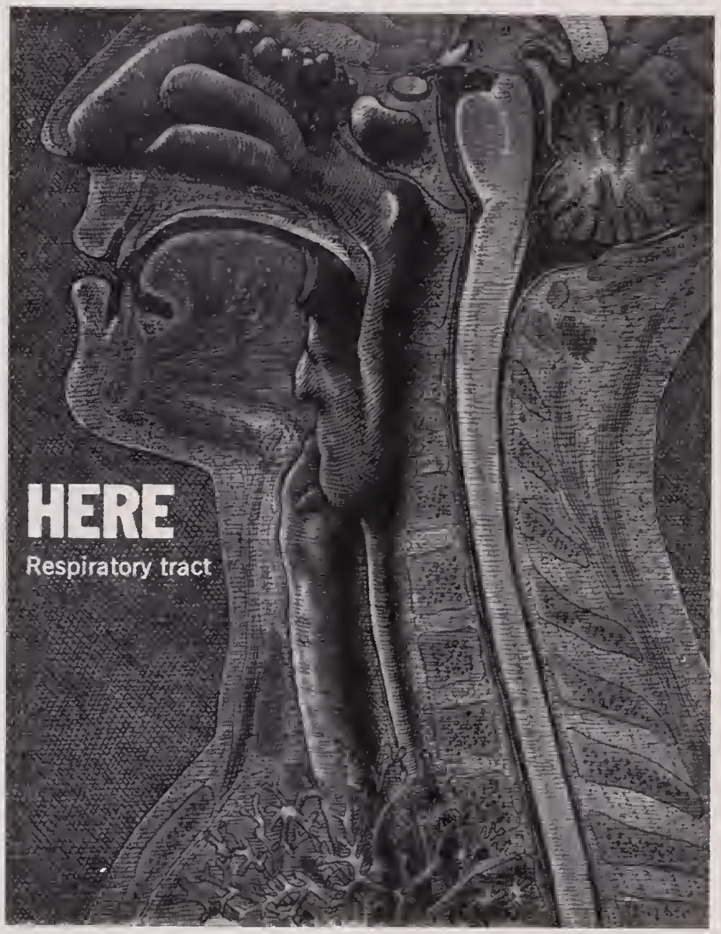

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Opinion & Dialogue

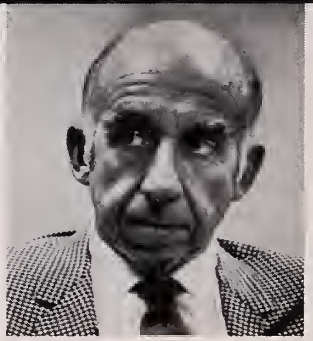
The Role of the Detail Man

Dr. Willard Gobbell
Family Physician
Encino, California

"I may be prejudiced, bu a
very much in favor of the deta ne
I meet. Most of them are know dg-
able about the drugs they pror te
and can be a great help in acq
ing me with new medication."

Family Physician's Perception

I think that most general
practitioners in this area feel a
do about the detail man. Over
years I have gotten to know mc o
the men who visit me regularly
they in turn have become awar of
my particular interests and th a-
ture of my practice. They, ther
fore, limit their discussion as r c
as possible to the areas of inte st
to me. Since I usually see the s ne
representative again in future
visits, it is in his best interest t
supply me with the most hones
factual, as well as up-to-date
information about his products


Dr. Jeremiah Stamler
Chairman
Department of Community
Health and Preventive
Medicine, and Dingman
Professor of Cardiology
Northwestern University
Medical School

"In the total picture of de n
with health problems in this co t
there is a potential for detail m
to play a meaningful role."

The Positive Influence

My contact with represen-
tives and salesmen of the phar
ceutical industry is the type of n-
tact that people in a medical ce e
research people, and academic
people have and that's in all lik ho
on a somewhat different level f n
that of the practicing physician

Let me touch on how I per n
ally perceive the role of the sale
representative. These men rea
large numbers of health profes
sionals. Thus they could be—a
at times actually are—dissemi-
tors of useful information. They
could consistently serve a real u-
cational function in their ability
discuss their products.

At present they do distrib
printed material, brochures an
pamphlets—some of it scientif
ally sound and therefore truly u-
ful—as well as some excellent ns
produced by the pharmaceutic
industry. When they function in is

a Source of Information?

Yes, with certain reservations.
average sales representative
great fund of information
t the drug products he is re-
sible for. He is usually able to
er most questions fully and
igently. He can also supply
nts of articles that contain a
deal of information. Here,
exercise some caution. I usu-
ccept most of the statements
pinions that I find in the
rs and studies which come
the larger teaching facilities.
s without saying that a physi-
should also rely on other
es for his information on
nacology.

ing of Sales Representatives

Ideally, a candidate for the
on as a sales representative
harmaceutical company
d be a graduate pharmacist
as a questioning mind. I don't
this is possible in every case,
o it becomes the responsibility of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

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city they are indeed useful;
cularly in the fact that they
minate broadly based educa-
l material and serve not just
ushers" of their drugs.

ther Side of the Coin

Obviously, the pharmaceuti-
mpanies are not producing all
aterial as a labor of love—
re in the business of selling
ucts for profit. In this regard
mbitious and improperly moti-
sales representative can
a negative influence on the
icing physician, both by pre-
ng a one-sided picture of his
ct, and by encouraging the
itioner to depend too heavily
ugs for his total therapy. In
ways, the salesman has often
ted objective reality and
mined his potential role as an
ator.

dustry Responsibility

Since the detail man must be
ormation resource as well as
esentative of his particular
haceutical company, he
d be carefully selected and thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.*, the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that information must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

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Editorials

Folate Deficiency Due to Oral Contraceptives

HE ARTICLE by Lewis* entitled, "Folate Defiiency Due to Oral Contraceptives" again points ut the need for careful evaluation of all patients rior to and during the use of oral contraceptives. here is no doubt that the low pregnancy rate ecorded using oral contraceptives and their conenience has made them a desirable form of conraception.

We must be reminded that oral contraceptives re drugs with potential hazards and thus they ust be prescribed using sound medical basis in hoice of drug, duration of use, and follow-up xaminations while on the drug. The package inerts in oral contraceptives carry warnings conerning relative risks. Despite these warnings any patients are placed on these drugs without ven a history and physical examination by their hysician to determine the suitability of the precribed drug for that patient.

All patients must be evaluated by history and hysical examinations before being placed on ral contraceptives. Those patients who are norally ovulating and have a normal physical examination can be given oral contraceptives for a limited period of time (six months to one year) after which re-examination is necessary. The use of oral contraceptives without a workup in a teenager who is anovulatory to regulate her menses must be condemned.

Careful follow-up demands annual physical examinations including blood pressure, with a minimum laboratory workup being a hemoglobin or hematocrit, urinalysis and pap smear. Questioning at the time of this evaluation should determine any side effects requiring a change in medication or its discontinuation.

Oral contraceptives are relatively safe and certainly effective drugs but they must be used carefully to avoid the undesirable side effects as noted in Lewis's article.

The routine use of a folic acid containing vitamin preparation as has been proposed by some drug companies will prevent the problem of folic acid deficiency anemia but can not substitute for careful follow-up of a woman on oral contraceptives.

Peter E. Fehr, M.D.
Minneapolis, Minnesota

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*See page 945.

Tumors of the Skin

T IS A PLEASURE to comment on the fine conribution in the October issue by Peter J. Lynch, M.D., titled "Tumors of the Skin."* The author's ather, Francis W. Lynch, M.D., is an eminent Minnesota dermatologist who has been interested in tumors of the skin for many years.[1,2] It is appropriate that his son, who received his medical education at the University of Minnesota, should participate in the continuing education of Minnesota physicians.

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*See page 780.

Common experience suggests that virtually everyone suffers from one or more benign skin tumors, ranging from common nevocellular nevi to seborrheic keratoses. In the United States, the prevalence of skin cancer among white people doubles every 265 miles nearer the equator. The patient with blue or grey irises or with red hair or freckles is much more susceptible than others. Patients of Celtic extraction, likewise, are more susceptible. Lynch and associates[2] reported an incidence (per 100,000 population) of 118.7 patients with skin cancer in Minnesota in 1963 compared to 191.9 in New Orleans in 1948,[3] 260 in Dallas in 1948,[3] and 422 in Tucson in 1969.[4] Surveys[5,6] have demonstrated an increase in the prevalence of skin cancer in the past two decades in the United States.

Minnesota has a large population of farmers and ranchers who are subjected to prolon exposure to sunlight as an occupational haza There is ample evidence that prolonged sunli exposure predisposes the fair-skinned individ to the development of premalignant and ma nant tumors of the skin.[1,7] Weary[8] has repor his experience with a series of skin and oral can detection clinics in rural Virginia communiti An overall detection rate of 20.1% for premal nant or malignant skin cancers was reported 548 patients examined. This examination w limited to the sun-exposed areas of the bo (from the clavicles upward and the elbows dov ward on the arms).

Family practitioners are presented with da opportunities to examine the sun-exposed sk of their patients. A wealth of treatable patholo awaits the eye that can distinguish the beni from the premalignant and malignant skin tumo

Roy S. Rogers III, M.I
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*Department of Dermatology, Mayo Clinic and Mayo Foundation.

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Senior Citizen

THE SENIOR CITIZEN HAS A low profile in contemporary society. Business interests are directed instead toward the "younger generation" whose problems also capture the attention of political and religious institutions, MINNESOTA MEDICINE'S article on "Perceptual and Psychological Changes in Aging"* presents a definitive model for rediscovering the Senior Citizen. Doctors—particularly the "Senior Physician"—have a vital stake in this research.

The implications of aging go beyond just physiological treatment of the older patient. Many doctors are familiar with psychological aging studies done prior to the 1950's. These cross-sectional investigations[1] report a steady decline of general intelligence scores, plus a con tinual decreased adaptability to new situation during an adult's life time. Many doctors, there fore, take a pessimistic approach to the olde patient. They may delegate him to a "rocking chair" role and a nursing home environment.

However, longitudinal studies of aging[3,4] ques tion the above conclusions. Studies of the sam individual done over a period of time indicat *increases* in intelligence and work abilities. In tellectual stimulation appears important for th continued growth of an individual, and stimulat ing surroundings seem important as a correlatior with *increased* performance and intellectua scores. Decline of mental ability does occur fo an individual in his seventies and eighties, bu individual differences are very great and ma ften outweigh the effects of age. It is important note that environment and time parameters for roblem-solving are crucial variables. A familiar, ilored environment (see article) coupled with inimal time pressures often lead the Senior itizen to as accurate solutions as they were able perform in their youth.

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*See page 614.

As physicians, we, too, will grow old and find ur perceptual and psychological resources taxed. he doctor who is a Senior Citizen has a unique sition that allows understanding and empathy r his peers. Medical education should be proded to allow this "Senior Physician" to be curnt in his practice skills. His schedule should low him the time to satisfactorily handle geriric problems. Recent revisions of Medical Reew Boards do provide protection for the comunity and the physician himself against adverse fects of aging on his quality of practice. The medical profession needs particularly to assist the "Senior Physician" meet the challenge of aging . . . in his practice and in his patients.

Peter Peth's proposed "efficiency model" (EM) gives us a measurable system to analyze geriatric patients. The problem with any computor or behavioristic model is that the factor of motivation lacks adequate description. "Reward and reinforcement" may not adequately describe the older patient's reliance on religious faith, on his enthusiasm for day-to-day living, and may neglect many social nuances that can make his life a pleasure. The "efficiency model" provides for scientific measurements, but the physician needs to add factors of empathy and optimism in dealing with the Senior Citizen.

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Cover Photograph

"Minnehaha Falls"

Dr. Bruce C. Nydahl took the cover photograph in the winter of 1965, in February or March of that year. The photograph is of Minnehaha Falls and there had been considerable melting and considerable water flow prior to that time. He has taken thousands of photographs over the years and now spends his time locally going out to take pictures of local scenes when the conditions are just right such as temperature, new snow fall, sunlight etc. The cover photograph was taken on one of these jaunts. The film was Kodachrome, and the camera was a Retina Reflex S.

Dr. Nydahl practices internal medicine in Minneapolis and his office is in the Southdale Medical Building. He went to medical school at the University of Minnesota and graduated in 1960. Most of his residency in internal medicine was taken in Minneapolis at the Veterans Hospital.

Annual Meeting

The Minnesota State Medical Association's annual meeting in St. Paul, May 21-23, 1975, at the St. Paul Hilton Hotel.

Letter to the Editor

Dear Editor:

This is written in appreciation of your August 1970 edition, in which you paid tribute to an X-POW, Leslie Caplan, M.D. May we infer that his early demise was directly the result of his wartime experiences.

Within the past month, a copy of MINNESOTA MEDICINE came to us from a former German POW. Careful reading permits one to understand the feelings of the gentlemen who prepared material for the Leslie Caplan Memorial Symposium, Minneapolis Veterans Administration Hospital, 3 September 1969.* Careful reading also tends to emphasize the quality of the effort and the value of the information presented.

As an X-POW, may I be so bold as to add a few thoughts and perhaps explain an item which may bother some readers? My background brings some elements of knowledge to this matter.

The writers seem confused by two factors pertaining to POW behavior in Korea. May I suggest, (a) that the Reds used the Turks as "window dressing" for examples of their generosity? The Turks were able to set up their own internal government, while this factor was denied the U. S. troops. (b) Many or most of the men were taken prisoner in the early stages of the war. Troops were thrust into the lines, or beach, or battle with no real experience or training (since basic training), no cohesion as to unit, whether it be company, battalion or whatever. (c) The units of the Second Division who finally stopped the Red Drive south, did it at great cost to themselves. Units were overrun after dogged defense, with the survivors surrendering only after they were out of ammunition and wounded. Further defense was useless. It may be noted that the Reds separated these men, the privates from their non-commissioned officers, removing any chance of organization.

The subject has not been well covered by either the military or the medical. MINNESOTA MEDICINE did the entire medical profession, as well as the general public, a definite service in its publication. Thank you for a fine effort.

Garry J. Anloff, Jr.
Chairman, Medical Research Committee
American Ex-Prisoners of War, Inc.

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*Pages 915-922, August, 1970.

It's the Law

$100,000 Judgment for Unnecessary Removal of Breast

A surgeon performed an operation on a woman to remove a cyst from each breast. The surgeon instructed the nurse to put both cysts in the same container and send them to Pathology. Both specimens arrived in Pathology in the same bottle. The Pathologist dissected them. One cyst was found to be malignant. Because the specimen's identity had not been preserved, both breasts had to be removed. The patient sued both the surgeon and the hospital for malpractice after a period. After a jury trial the court awarded her a judgment of $100,000. The court said that the evidence was that the negligence of the surgeon and hospital were so intertwined that they were a single cause of the patient's injury. Both hospital and surgeon were deemed negligent and liable for damages.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Variety Children's Hospital v. Osle, 292 So. 2d 382 (Fla. Dist. Ct. of App., April 2, 1974).
The Citation 29:9, August 15, 1974.

Thermogram and Mammogram

THIS 54-YEAR-OLD woman participated in a thermographic breast screening program. She was asymptomatic. The resultant examination is shown in Figure 1.

The equipment is calibrated such that areas of increased skin temperature appear light on the photograph. Which breast is abnormal? What is your diagnosis?

What should be done next?

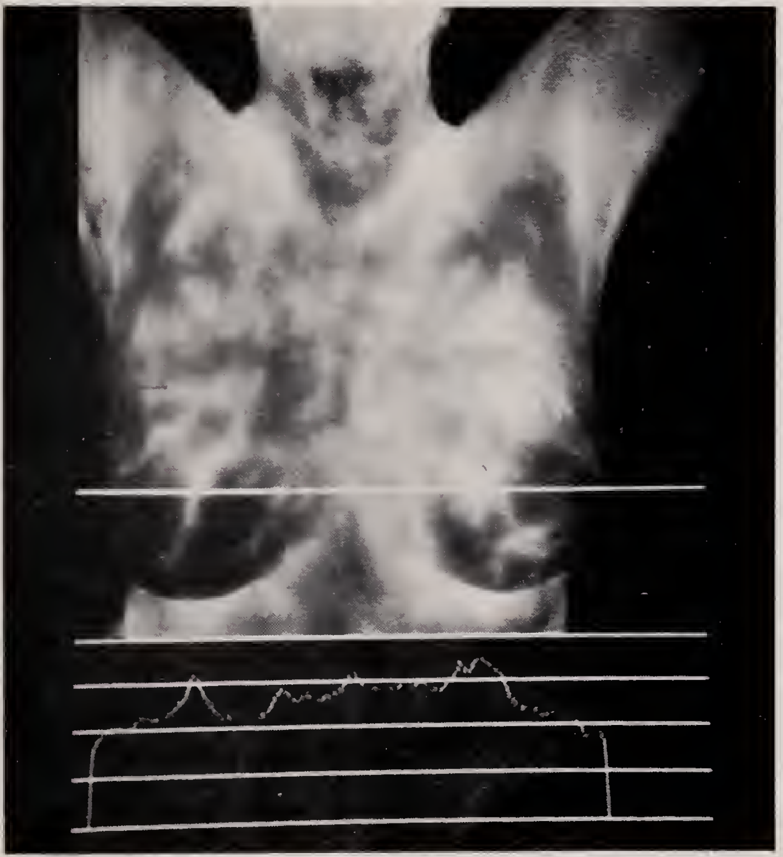

Fig. 1—Thermogram.

Diagnosis

The thermogram demonstrates generally increased temperatures in the upper outer quadrant of the left breast. While this is non-specific, carcinoma must be excluded.

The breast was normal to palpation. A xeroradiographic mammogram showed no mass or other malignant changes except for a small cluster of punctate calcifications in the left upper outer quadrant (Figure 2). This was reported as suspicious for cancer.[1]

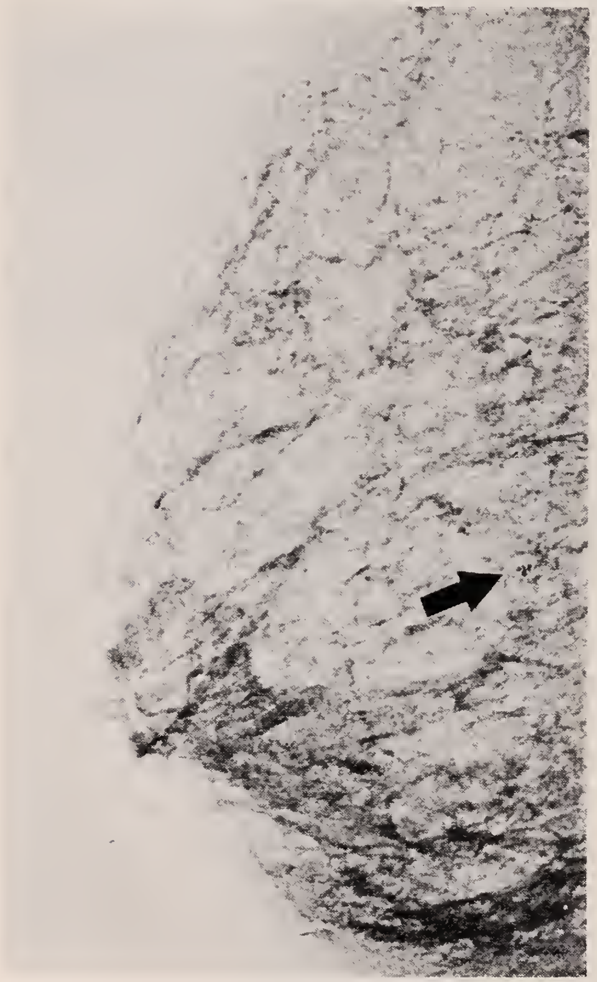

Fig. 2(a)—Xeromammogram left breast. Small cluster of punctate calcifications. (arrow)

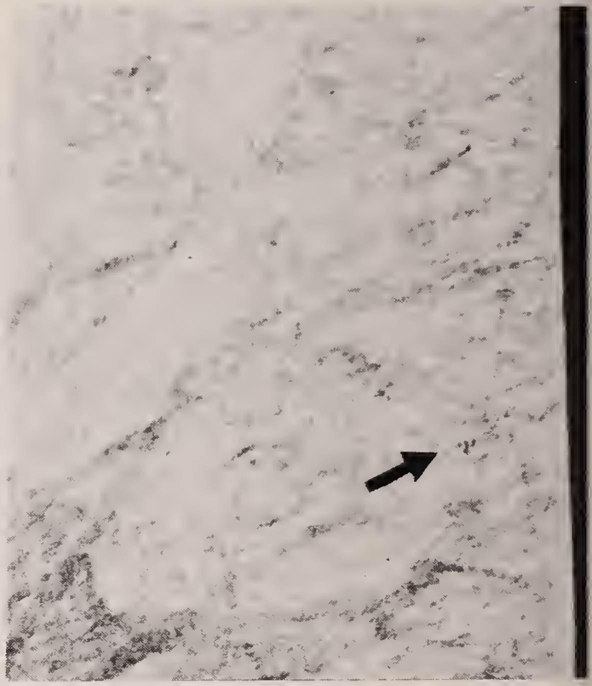

Fig. 2(b)—Xeromammogram close-up. (Arrow indicating calcifications).

Excisional biopsy of the involved quadrant was performed, and the specimen immediately xeroradiogramed to insure inclusion of the calcifications (Figure 3). The radiologist assisted the pathologist in localizing the suspicious area for the frozen section. The frozen section was interpreted as negative for malignancy. However the permanent sections showed focal areas of intraductal carcinoma adjacent to these calcifications (Figure 4). A radical mastectomy was performed which demonstrated no residual malignancy in either the breast tissue or regional lymph nodes.

The general principle upon which thermography rests is the empirical observation that focal malignant processes sometimes generate measurably more heat than normal surrounding tissue.[2-4] Recently developed instrumentation is becoming

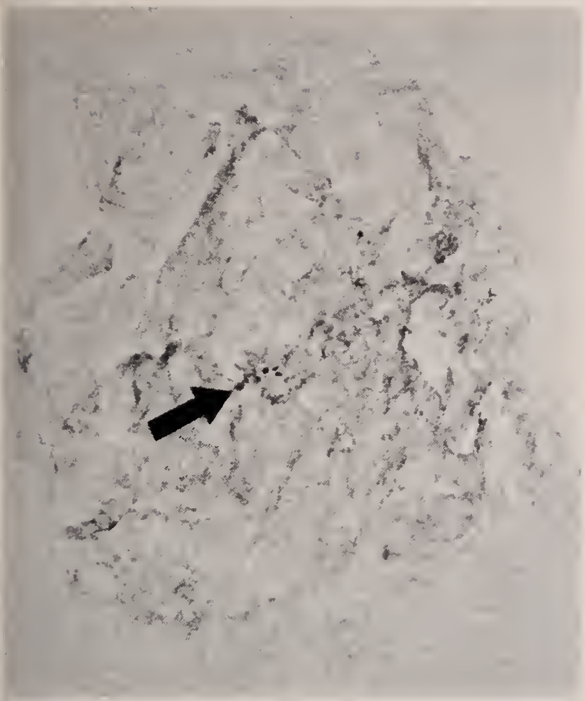

Fig. 3—Xeroradiogram biopsy specimen. (Arrow indicating calcification).

Fig. 4—Histologic section. Calcification with malignant intraductal cells.

available which is capable of resolving temperature differences as little as 0.2°C.

The patient disrobes to the waist in a room with a carefully controlled thermal environment for ten to fifteen minutes and is then examined in front of the measuring device for a few seconds. Surface temperatures are recorded and converted into an image on film. Since nothing touches the patient it is non-invasive. The study can be repeated as often as desired since there is no radiation or other hazard. Thermography is more quickly accomplished and less expensive than standard or xeromammography. At present thermography is unable to diagnose cancer with the degree of reliability required to make it useful for direct screening for breast biopsy. It helps separate normal from abnormal breasts in asymptomatic females. Those with suspicious thermograms require rigorous investigation, including detailed palpation, and standard or xeromammography.

Some false negatives occur, and many false positives are seen.[5-8] Most of the latter represent normal variation or benign pathology upon further evaluation.

Current studies indicate that an asymptomatic population will yield positive thermograms in 24-31%.[5-7] When thermography is utilized as the first screening test and followed by mammography in suspicious cases, the detection rate for malignancy in the screened group is about 21 per 1000 mammograms.[7] This compares with a rate of 1.6 to six per thousand for mammography screening alone.[9-14] In asymptomatic groups screened simultaneously with both modalities the yield is 7.3 to 8.5 per thousand.[7,15] Its value can be appreciated when one considers the detection rate of two to 15 per thousand which has justified the use of the cervical cytology in mass screening for carcinoma.[16]

Standard and xeromammography can often localize nonpalpable lesions, frequently discriminate between benign and malignant processes, and accurately determine the best surgical biopsy site.

The thermogram fulfills the basic requirements for a mass screening technique. It is convenient and safe. It is quickly performed, averaging twelve minutes in experienced hands.

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Acknowledgment

Assistance in preparation of these reproductions by Steven Jamison, R.T. is gratefully appreciated.

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The Low Incidence of Chronic Primary Open Angle Glaucoma in the Chippewa (Ojibwa) Indians of Minnesota

JAMES R. THOMPSON, M.D.* and IRVIN H. HARPER, B.A.*

An isolated ophthalmic practice permitted an incidence study of ocular disease in the Chippewa (Ojibwa) Indians of Minnesota. Although the Caucasian population demonstrated an expected number of cases of chronic primary open angle glaucoma, no cases of this type of glaucoma were diagnosed in the Chippewa.

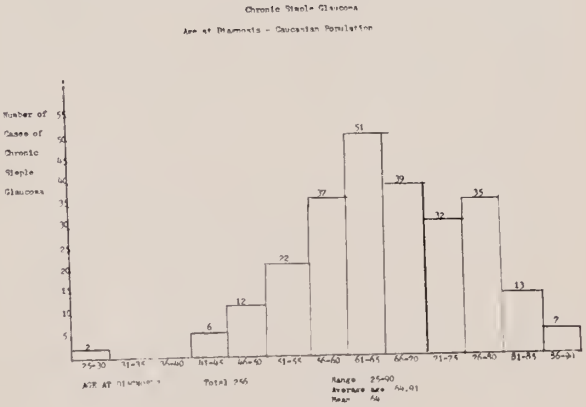
THE SENIOR AUTHOR practiced ophthalmology among the Navaho Indians during 1966 at Fort Defiance, Arizona. He found a low incidence of chronic primary open angle glaucoma affecting these people, as others have reported.[1] He began private practice in 1966 as the only ophthalmologist in Bemidji, Minnesota, and continued the study of chronic primary open angle glaucoma in the American Indians.

Bemidji lies in the center of a triangle of three Chippewa (Ojibwa) Indian Reservations and is the medical referral area for all three. Thirty-five miles north is the Red Lake Reservation with a population of slightly over three thousand and their own United States Public Health Service (USPHS) Hospital. About twenty miles east begins the Leech Lake Reservation with approximately two thousand three hundred Chippewa Indians and a USPHS Hospital at Cass Lake, Minnesota. Southwest is the White Earth Reservation with a population of twenty-five hundred.[2] The plan was to compare the incidence of chronic primary open angle glaucoma in these eight thousand Chippewa Indians with the Caucasian population of about 45,000, in the same geographic area.

The Indian population has been well screened for glaucoma. Ocular examinations have been done on approximately fifteen hundred of the Chippewa Indians by the authors. During the period from 1967 to 1973, residents in ophthalmology from the University of Minnesota did 5137 eye examinations at the Red Lake and Cass Lake USPHS Hospitals under the supervision of the senior author. The Public Health Service physicians at the three reservations have referred any patients suspected of having ocular disease.

For this study, chronic primary open angle glaucoma is not diagnosed without typical visual field loss unless the initial applanation intraocular tension is greater than 30 mm Hg. Acute angle closure, secondary, and congenital glaucomas have not been considered in this study. During the seven years under consideration 256 cases of chronic primary open angle glaucoma in the Caucasian population of about forty-five thousand have been diagnosed.

During these seven years not one single case of chronic primary open angle glaucoma has been seen in the Chippewa Indian population. There are two Chippewa Indian patients who demonstrated borderline intraocular pressures with no disc or field changes, but who were lost to follow up. The occurrence of 256 cases of chronic primary open angle glaucoma among 45,000 Caucasians compared with no cases among 8,000 Chippewa Indians is highly significant.



Figure

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*Bemidji, Minnesota.

It has been argued that the American Indian does not live long enough to manifest glaucoma. Of all patients screened for this study, the average Caucasian age is 35.9 years and the average Chippewa age is 35.1 years. Life expectancy figures for the Chippewa Indian population of Minnesota are not in existence, but the life expectancy for the Indian and Alaskan natives in the twenty-four reservation states was 64.9 years in 1970, compared with 71.3 years for the Caucasian population of the United States.[3]

The 256 cases of chronic primary open angle glaucoma were tabulated as to age at diagnosis. As the figure illustrates, there was a bell shape curve in regards to the age at diagnosis of glaucoma with a range from twenty-five to ninety. The mean age was sixty-four, which would put the age at diagnosis of approximately half of the Caucasian glaucoma patients within the calculated life expectancy of the American Indians.

Summary

This Minnesota population of Chippewa Indians has been well screened for chronic primary open angle glaucoma, and no cases have been diagnosed. The respective Caucasian population has demonstrated an expected number of cases of glaucoma. A tabulation of the age at diagnosis for glaucoma in the Caucasian population illustrates that the Chippewa do live long enough to manifest glaucoma. This incidence difference between the two populations is significant, and it is presented with the thought that further investigation, possibly a genetic study, may be initiated.

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Harold S. Diehl Award

The Alumni Association of the University of Minnesota Medical School presented the Harold S. Diehl Award to Ann Whelan Arnold, M.D., Roger MacDonald, M.D., Carl O. Rice, M.D. and Ragnvald S. Ylvisaker, M.D. at its 37th Annual Meeting held in October.

The award is presented to practicing physicians who have made outstanding contributions to either the medical school, the University, the Alumni Association or to medicine in the State.

Treatment of Obesity*

A Behavior Modification Approach

GLORIA R. LEON, PH.D.†

Significant weight loss has been reported in a number of studies employing behavior modification procedures in the treatment of obesity. Behavioral methods for treating obesity are based on the premise that excessive overeating (excluding metabolic disorders) is an overlearned habit that has generalized to many stimuli and environmental events unrelated to physiological cues of hunger. Behavior modification procedures attempt to change the individual's eating pattern by reducing the number of inappropriate stimuli that are responded to with food intake. Specific techniques are described which help one limit the amount of food consumed and teach one to restrict eating to appropriate times and places. The use of self monitoring of food intake as a means of obtaining baseline information and as a tool of behavior change is also discussed. A point system procedure for motivating the person to change his or her eating patterns was described and suggestions were given for the implementation of this procedure.

WITHIN THE PAST FEW YEARS, there has been an increasing number of reports on the use of behavioral methods derived from experimental psychology for treating the problem of obesity.[1-7] These studies found that significant weight loss occurred when the problem eating behavior was modified through systematically applying the principles of learning theory. Stunkard[8] reviewed a number of the studies employing behavioral treatments for obesity and concluded that behavior modification is more effective than previous methods of treatment. The evidence therefore suggests that a symptom oriented treatment focused on directly teaching the obese person how to modify one's eating pattern can be an effective form of therapy.

Overeating May be an Overlearned Habit

A learning theory analysis of obesity (excluding metabolic disorders) considers excessive eating as an overlearned habit, i.e., a strongly conditioned response to diverse environmental stimuli. Such stimuli include various kinds of emotional arousal, loneliness and boredom, anxiety provoking interpersonal situations, or other social interactions.[9,10] The consumption of food in response to these stimuli may have resulted in anxiety reduction or positive gratification in the past, and therefore the frequency of eating in these situations gradually increased. Thus, a learned association developed over time between various stimuli and food intake and eventually, these stimuli or events became cues for eating behavior. The conditioning process further strengthened and generalized as numerous situations in the individual's life became associated with food intake. Thus, the goal of a learning oriented treatment is to modify the obese person's behavior by reducing the number of inappropriate stimuli that he or she responds to by eating. The individual eventually can learn to respond with food intake to the more appropriate physiological cues of hunger.

Constitutional factors, if present, probably operate in a complex interaction with the factors of reinforcement and imitation learning. It is possible that a specific individual of a particular genetic endowment may also have experienced a learning history characterized by reward or approval for overeating. In addition, if one or both parents are obese, that parent may have modeled patterns of overeating which the individual then adopted. The variables of constitution, reinforcement, and modeling may all interact simultaneously.

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*Portions of this paper were presented at a Central Minnesota Area Health Education Consortium (AHEC) Workshop on March 8, 1974 at the College of St. Benedict, St. Joseph, Minnesota.

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Treatment Approach

The learning approach to obesity contrasts with the traditional psychodynamic formulation of excessive overeating as the result of unresolved oral dependency needs. However, irrespective of whether the reader views obesity as a habit disturbance or a problem of psychopathology, treatment may be more effective if the eating behavior, per se, is dealt with.

Behavior modification procedures for treating obesity have been most effective when focused on changing the individual's eating patterns.[5,11] A reduction in the number of calories consumed per day and concomitant reduction in weight will automatically occur if the obese person assumes an eating pattern based on consuming three balanced meals per day and refraining from high caloric snacks. If treatment is not oriented around the number of pounds lost per week, the therapist can avoid the tendency of some patients to crash diet before a scheduled appointment and then revert back to the typical pattern of overeating until close to the time of the next appointment. Paying attention to the environmental and emotional circumstances in which eating occurs and instructing the patient how to change this stimulus-response pattern can result in the learning of new and effective skills for limiting one's eating behavior. The learning of these skills appears to be a crucial element in the successful maintenance of a weight loss.[12]

Monitoring Activities

In order to achieve a modification of eating behavior, it is extremely important to obtain baseline information about the patient's pattern of food intake. I have found it quite useful to have the patient record on a standardized questionnaire[10] all of the circumstances in which eating occurred over a 24 hour period. The patient is instructed to complete the forms on three days, with one of the days falling on the weekend. Along with the information the therapist obtains about the eliciting circumstances associated with food consumption, the process of monitoring also focuses the patient's attention on the frequency of eating in these situations. On the basis of the information obtained from the monitoring forms, one can teach the patient a number of substitute, incompatible behaviors to engage in while in the process of unlearning the habit of inappropriate eating. For example, if a patient typically eats during the afternoon while watching television, it would be helpful to counsel that person to take a walk each afternoon when he or she feels like eating, or work on a project where one has to use one's hands.

Changing Patterns

Stuart and Davis have made an extremely important contribution to the behavioral control of obesity, with the publication of their book *Slim Chance in a Fat World*.[11] The authors outlined a series of steps which they have found effective in modifying problem eating patterns. They stated that it was very useful to include significant persons in the patient's social environment in the planning and monitoring of the weight reduction program, so the patient could gain the emotional support and encouragement of these persons. Probably the most difficult step, however, was to make eating a "pure activity," engaged in at specific time periods each day, i.e., regular meal hours, and in a specific place in the home. If food consumption is isolated from other activities, the learned association between eating and watching TV, reading, or conversing with others can eventually be broken.

Stuart and Davis pointed out that the process of unlearning can be expedited if problem eating is made as difficult as possible. The patient can be instructed to remove food from locations in the home other than the kitchen, and also reduce the availability of foods that can be eaten without preparation. When food is prepared, it can be served in small portions so a second helping requires the effort of getting up from the table and preparing another portion. The authors indicated that contact with excessive food through serving "family style" should be avoided. Small portions of food can be made to appear as large as possible by using a smaller plate and spreading the food out on the plate.

Many obese persons eat quite rapidly, and therefore the process of relearning should also focus on slowing the pace of eating. This can be accomplished by instructing the individual to take small bites or mouthfuls of food and chewing thoroughly and swallowing all the food in one's mouth before taking in any more food. Stuart and Davis further suggested that the patient leave the table if he or she finishes before the other family members. The person can then come back later for dessert, and avoid sitting at the table confronted with the temptation of consuming more food because other persons are still eating.

The obese individual can be counseled to avoid purchasing foods that are high in caloric content and associated with problem areas, e.g., potato chips which that person typically consumes while watching TV. It may be easier for the patient to refrain from purchasing these foods if grocery shopping is done from a list which is strictly adhered to, or if the individual takes only a given amount of cash to the grocery store. In cases where it is extremely difficult to avoid purchasing problem foods, it may be necessary for another member of the family to do the food shopping.

Other Important Factors

Although therapy aimed at modifying eating patterns is important, other procedures are necessarily part of a total treatment program. The individual should have enough nutritional information available to be able to choose acceptable foods to eat and monitor the amount of food consumed. Balanced and regular meals are also important in controlling states of deprivation leading to excessive eating. For many persons, sleep deprivation may be a cue for food intake, so adequate sleep will help to limit inappropriate eating behavior. A regular exercise program is also quite useful in the process of weight reduction and weight maintenance.[13]

Reward and Penalty System

Recent studies have found that a combined reward and penalty system was the most effective procedure for motivating the individual to change one's eating pattern. Mann[6] and Jeffrey and Christensen[7] reported a reward and punishment system arranged so the person deposited a given amount of money with the therapist and earned back set amounts of money for each pound lost. Weight gain resulted in the permanent loss of a specified amount of money, which was then sent to some type of organization.

Alternative Point System

A reward-penalty system can be applied in treatment by instructing the patient to keep a daily record of whether given eating pattern changes occurred, i.e., no eating between meals, eating only allowable foods, eating at regular hours, and eating only in a specified place. The person can then award oneself a point for each behavior complied with and accumulate points toward prearranged goals. Thus, the patient can specify that a given number of points must be earned in order to go to the movies, buy an article of clothing, or engage in any other meaningful activity not associated with food. The daily number of points earned can serve as an immediate reward as well as provide feedback of progress, while the accumulation of points for a delayed reward sustains the eating pattern changes over a period of time.

Group Support

The point system procedure can also work well in a group setting, by having each person bring one's records to the meeting. Through participating in a group, the obese individual can gain the social support of other persons who are undergoing a similar change in life style in relation to food. The members of the group can also function as a source of peer pressure to induce the individual to accomplish a change in eating patterns.

Emphasis on Pattern Change

The person who is in the process of losing weight may find it helpful to keep a daily graph of pounds lost and in this way monitor progress. However, Mahoney[5] found that obese individuals who provided self reward for habit change showed more pronounced improvement than persons who provided self reward specifically for weight loss. Therefore, the emphasis of discussion with the therapist should be oriented around eating pattern changes, rather than number of pounds lost.

Depression Infrequent

The emotional distress and depression noted in some individuals in the process of or upon accomplishing a substantial weight loss has not been reported with the use of behavior modification techniques. The apparent infrequency of severe emotional distress may be due to the use of reward systems and goals to modify the eating behavior. These procedures provide the individual with a personally gratifying incentive to strive for, and removes the therapist from the primary role of depriving the patient. Instead, alternative behaviors are learned and the individual can gain substitute satisfaction from activities not oriented around food consumption.

Long Term Goals

Through the self monitoring of successful changes in eating patterns, the patient gains a feeling of mastery and perhaps an increased sense of self esteem. For many persons with obesity problems, guided education on how to change one's eating patterns may therefore be an effective means of achieving and maintaining a weight loss over an extended period of time.

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Bloom's Syndrome

The presence of telangiectatic erythematous areas resembling lupus erythematosus that occur over the face in Lorain-Levi dwarfs has been described by Bloom. Crusted bullous lesions were also present on the lips. The manifestations appeared during the first few years of life and were essentially identical in three cases. Another patient had a variety of additional cutaneous lesions.

Durham, Robert H.—Encyclopedia of Medical Syndromes
Hoeber Medical Division, Harper and Row, New York

It is most common for the doctors to err (or pretend to err) in the case of the sick on the side of hopefulness. They say, "We have seen persons even worse, who have got over it: we are not prepared to say there is no hope" (indeed, when they are prepared to go to that length, matters are serious indeed).*

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*James Payn: A Grape from a Thorn. Chapter 28 "Dying Words." 1881.

General Considerations in the Interpretation of Clinical Laboratory Data

PHILIP BLUME, M.D.*

If laboratory medicine is to make a major contribution to clinical medicine—apart from the present services it provides—it should be through the solution of the problems discussed as a route to improved diagnosis and patient management.

THE RELATIONSHIP of a disease state and those patient variables which can be evaluated by the clinical laboratory is central to the field of laboratory medicine. These relationships and the laboratory measurements with which they are associated have become highly significant to the contemporary practice of medicine. The role of laboratory medicine must transcend the acquisition of data and incorporate aspects of clinical interpretation and diagnosis. The extent to which this occurs will significantly determine the extent to which medicine will benefit from many of the technological developments that are transforming laboratory science.

Most discussions of clinical interpretation of laboratory data appropriately deal with specific organ systems and related pathophysiology. How may we best diagnose hypo- or hyperthyroidism? What is the significance of plasma estriol levels in establishing the viability of a pregnancy? How may we best utilize laboratory analyses to diagnose diabetes or renal disease or myocardial infarction?

These are questions discussed among all clinicians and are certainly central to the thoughts and goals of laboratory medicine. But to discuss them in one brief article would amount to reducing the practice of medicine to a few pages. Throughout all of the applications of laboratory measurements there are certain themes which recur again and again. From the perspective of the laboratory we are in a favorable position to appreciate these themes and, in doing so, enhance the contribution of the laboratory to the practice of medicine.

Let us invoke a hypothetical situation. Assume that as a result of accumulated clinical experience or basic experimentation, a relationship is established between a condition which we may call "disease X" and the serum level of a compound (SLX). For simplicity, let us assume that deviations in SLX are confined to abnormal elevations although we can immediately think of important examples where this is not true.

Upon deciding that an SLX assay will aid in the diagnosis of disease X we first establish an assay technique that is suitable for routine application and is "good enough for clinical use." We next determine a "normal range" for SLX by collecting a number of specimens from blood bank donors who, to the best of knowledge and clinical judgment, are healthy. We carry out the assays and calculate the mean value and the standard deviation. Plus and minus two standard deviations about the mean will include 95 percent of the population, and since 95 percent strikes us as a reasonable number of people to be normal, we call this our "normal range." Later, on a suitable patient, we determine the SLX and check our "normal" value table. Using this information and other laboratory data, as well as the history and physical examination, we come to some conclusion as to the patient's status. Finally, since disease X, it is thought, will have a more benign course if detected early and treated immediately, we decide to add a routine SLX determination to our multiphasic screening procedures. It might even be decided that since this assay will only be a "rough screening procedure," we need not expend as much effort in obtaining as precise a value as we might otherwise require.

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The normal values were derived from a group of blood donors which, in our institution is likely to consist of predominantly young and male subjects. Unfortunately, if SLX is similar to many other laboratory determinations in common use, it may normally vary significantly with age and sex. For example, a cholesterol level of 245 mg/dl represents the mean for the 50-59 year age group yet would be outside of the 90 percent range for anyone under thirty years of age.[1] When we report a result, we should also be able to provide, a specific interpretation of the degree of abnormality based upon the individual's age and sex. This sort of personalized data evaluation is feasible with a laboratory computer reporting system although the necessary data base is difficult to obtain. Careful standardization of laboratory methodology and consistency from one institution to another could provide enough data from large groups to collect this necessary data base providing that we realized the possible existence of true geographic variations.

Age and sex are not the only variables which affect physiologic measurements within a normal group of individuals. Many variables are subject to periodic variation. For example, in diurnally active people, 17-hydroxycorticosteroids are usually much higher in the morning than at midnight.[2] Not only are rhythmic variations characteristic of health, but their alteration or absence is an indication of disease; in Cushing's syndrome the normal circadian variation in 17-hydroxycorticosteroids may disappear.[3] Future modes of laboratory diagnosis may include the measurement of daily fluctuations in physiologic variables, as suggested by Halberg at the University of Minnesota and other investigators. The observed variations, in many instances, are the result of superimposed higher frequency variations and do not represent a simple circadian rhythm.

We frequently collect samples at a particular time of day because we know that they are subject to significant periodic variation. This provides only a single result from a single point in time and might falsely be interpreted as normal. A periodic function has properties beyond such instantaneous values. It has a frequency (or several frequencies, as indicated above) as well as time relationship that in the foreseeable future may offer the earliest indication of a pathological condition before alterations in amplitude or overall average values occur. Moreover, aside from diagnostic uses, therapy may also be timed according to measured rhythms.

Getting back to our model situation, let us consider the way we calculated the "normal range." Elveback[4] reminds us that Gauss, a mathematician, physicist and astronomer, was talking about the distribution of *errors*—errors made during repeated measurements of the same physical object, such as the measurement of the length of a desk top. The distribution of values will produce the familiar bell-shaped or gaussian curve and *if* a distribution obeys this equation, the standard deviation of the curve can be used to delineate definite portions of the sample values.

For example, as we have noted, the range of values from two standard deviations below the mean to two above will include 95 percent of the population if the length of a desk top has anything to do with the distribution of values of SLX in the normal population. The SLX values may by chance approximate a gaussian distribution, as in the case of serum albumin. However, as in the case of serum alkaline phosphatase, the distribution may be so highly skewed that it is necessary to plot the frequency of measurements against the *logarithm* of the measured values to arrive at something resembling a gaussian distribution. Therefore, the use of the standard deviation to establish a certain percentile range, e.g., the 95th percentile range of normals, cannot be assumed to be valid until it is demonstrated to be correct.

Furthermore, even if the distribution is normal, or if we employ a transformation to make it normal, or if we use completely different techniques to establish the range of values which encompass 95 percent of the population, we are still left with something of a dilemma. Five out of every 100 of our *normal* subjects are abnormal by this definition of "normal range." One alternative is to construct a percentile table from our set of values.[5] This may be done without any special reliance upon the shape of the distribution. Thus rather than indicating that a serum potassium of 5.2 meq/l is abnormal, we state that it is at the 97.5th percentile. Only 2½ percent of the normal population have potassium values above this level—but they do exist. This may not be as comforting as "knowing" that the level is abnormal but perhaps it is more realistic.

There are considerations to be taken into account before the specimen is collected. The fasting state is not necessary for all determinations but may be extremely important in others. For example, in the case of some serum lipid analyses, not only is fasting indicated prior to the analysis but a normal diet of proper caloric balance should be maintained for two weeks prior to the study.[6] Recently, Statland et al.[7] have shown significant effects of eating on serum sodium, phosphate, uric acid, iron total lipids, alkaline phosphatase and lactate dehydrogenase. They also found significant affects of prior exercise on serum potassium, phosphate, creatinine, total protein, albumin, uric acid and alanine aminotransferase.

Posture is an important variable during sample collection. When a subject moves from the recumbent to the standing position, a 10 percent decrease in plasma volume may occur, with a corresponding increase in the concentration of serum constituents.[8]

The sample of venous blood must be collected without excessive stasis and without producing hemolysis. It must be processed promptly and in a way that avoids artifactual changes prior to analysis. In the absence of a preservative, clotted blood sample kept at room temperature will display a significant decrease in glucose concentration. In one study the glucose concentration fell from 116 to 92 mg/dl in one and a half hours at 25°C and fell to 80 mg/dl in three hours. The same study showed that while refrigeration slowed the rate of glucose loss, it increased the rate at which the serum potassium rose, since the enzymatic processes which maintain the transmembrane potassium gradient were hindered.

Drugs may have several kinds of affect on the results of laboratory analyses. A drug in a specimen may interfere chemically or spectrophotometrically with the laboratory determination. A good example would be the affect of administered iodine upon the determination of protein bound iodine. The affect is strictly an analytical error due to the non-specificity of the method. If at all possible, analytical methods should be as free as possible from such potential sources of error. The use of specific assays to determine thyroxine levels largely solved this particular problem. On the other hand, a drug may produce a true physiologic response which our analysis detects. Knowledge of the presence of a drug is necessary in order to arrive at a valid diagnostic conclusion. For example, a patient taking oral contraceptives may display a significant elevation of serum thyroxine concentration. This is a valid analytical observation. However, the knowledge of the presence of the drug as well as its affect upon the level of thyroid binding globulin is necessary to lead us toward the diagnosis of the euthyroid state.

Of course, a drug may produce an affect which is exactly what it appears to be. A patient taking diuretics who is found to have a low serum potassium *is* hypokalemic. A patient who receives a hepatotoxic drug and displays an elevated serum transaminase activity probably does have liver injury. The interested reader is referred to the October 1972 issue of *Clinical Chemistry*. The entire issue is devoted to a computer generated index of drug affects prepared by Young and associates at the National Institutes of Health. Again, speculating about the future, files such as these may be incorporated into the laboratory computer to investigate automatically the possibility of drug-related variations in laboratory measurements.

Returning to the question of analytical accuracy we shall consider a study conducted at the National Institutes of Health.[10] A large number of measurements of fifteen serum constituents were made on specimens collected from a group of individuals who were followed over an extended period of time. The best clinical laboratory methodology available at the time was employed. Using techniques for the analysis of variance, the investigators separated the affects of analytical error, day-to-day variation within a single individual (intraindividual variation) and variation among the individuals within the group (interindividual variation). In almost all cases, the intraindividual variation of most assayed substances was less than the interindividual variation. Furthermore, the analytical variation exceeded the biological variation for precisely controlled constituents such as calcium. Thus a normal person can maintain his physiological variables within closer limits than the population as a whole. This suggests that significant diagnostic information may be derived by looking at departures from an individual's own baseline values obtained in time of health. However, this exciting idea can be proven (or disproven) only if sufficient care is given to the quality of laboratory analyses, so that we may be able to detect the degree of intra-individual variation.

Let us come to the matter of a screening assay for SLX to establish the early diagnosis of disease X in an otherwise healthy population. In most cases (Figure 1), an overlap exists between the distribution of values for healthy individuals and the population with the disease. Let us assume that we are talking about true distributions of values within the population devoid of any analytical or other variation. The problem is deciding which individuals have to be treated or evaluated more completely. We see that we have a "trade-off" situation between a predominance of false positive (if the normal limit is set at A) and false negative (if the normal limit is set at B) evaluations. We cannot tolerate an excessive number of false negative evaluations since the whole purpose of the program is to detect early onset of disease. However, moving our "upper limit of normal" from B to A results in an increase in false positive evaluations. These individuals must be evaluated and consideration must at least be given to the anxiety, if not neurosis, these individuals may suffer, as well as the possibility of iatrogenic morbidity if they are treated unnecessarily.

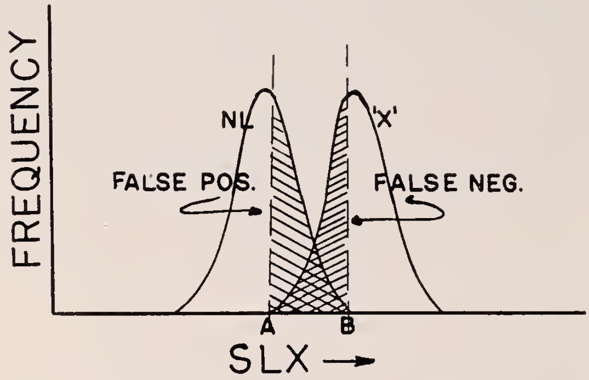

Fig. 1—Theoretical distributions of values of SLX in normal individuals and those with disease X assuming no analytical error. A and B represent two possible choices of "upper limit of normal."

We have just invoked a situation which was completely devoid of analytical error. But our initial scenario called for the use of a "rough screening procedure." It is unfortunate, but the word screening has at least two different connotations. We may think first of the comatose diabetic person who is brought to the emergency room. Is his serum glucose 900 mg/dl or 30? A rough but rapid screening test may be useful (if not in an equivocal range). But this differential diagnostic situation has little to do with screening healthy populations. What happens when we take our true distribution of measured values and superimpose upon each measurement an increased analytical error[11] (Figure 2). The effect upon the screening dilemma is clearly to make matters worse. The error simply spreads the two distributions and makes the overlap even worse. It seems clear that there is no justification for making any compromise with analytical quality because a procedure is to be used as part of a screening program.

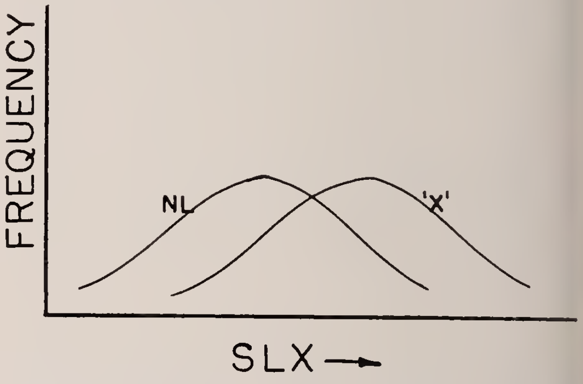

Fig. 2—Distributions as shown in Figure 1 but with superimposed analytical error.[11]

Finally, what happens when we do multiple test screening? Let us assume we have twelve nicely behaving distributions of normal values obtained with instruments of perfect accuracy. We need a criterion for calling any test abnormal and we fall back upon the 95 percent range. Thus for any single test, the chances of a normal person being called abnormal are five percent. From that time on it is like playing Russian roulette. By the time we have done 12 determinations, a normal individual has a 46 percent chance of being abnormal in at least one test. This is just the result of the simple arithmetic of probability. That means a great deal of followup examinations —too many for all but the most enthusiastic screeners. The significance of this dilemma can be illustrated by the curious suggestion[12] that when more than one test is done, the "normal range" for each be broadened so that no matter how many tests are done, only five percent (again that magic number) of individuals will be abnormal in at least one of the procedures!

These arguments apply principally to the mass screening of healthy individuals which has become fashionable with the availability of instruments capable of economically doing the work.

The situation may well be different for carefully performed admission procedures on hospital patients, in which case we start with a high incidence of pathological conditions and the cost of the battery can be weighed against the possibility of shorter hospital stays. We must also consider the utility of screening procedures specifically designed to accurately detect serious conditions whose outcome can be beneficially altered by early therapeutic intervention.

Again speculating about the future, multiple laboratory analyses have a more exciting potential role. That role is their utilization as organ or disease specific batteries interpreted by the techniques of multivariate analysis.[13,14] Using modern data processing techniques, rather than dealing with one value as a point on a line, we can treat n variables as the coordinates of points in n-dimensional space. We can then look for clusters of points associated with particular conditions. These and similar techniques may prove extremely useful in the future by enhancing our ability to interpret clinical laboratory data.

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Sir Dudley North, too, informs us, (or is it his brother Roger? but I mean the Turkey merchant)—that at Constantinople the respect for printed books is so great, that when people are sick, they fancy that they can be *read* into health again; and if the Koran should not be in the way, they will make shift with a few verses of the Bible, or a chapter or two of the Talmud, or of any other book that comes first to hand, rather than not read something. I think Sir Dudley says, that he himself cured an old Turk of the toothache, by administering a few pages of "Ovid's Metamorphoses;" and in an old receipt book, we are directed for the cure of a double tertian fever, "to drink plentifully of cock-broth, and sleep with the Second Book of the Iliad under the pillow." If, instead of sleeping with it under the pillow, the doctor had desired us to read the Second Book of the Iliad in order that we *might* sleep, I should have had some faith in his prescription myself.*

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*Matthew G. Lewis: Journal of a West India Proprietor, 1834.

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Minnesota Radiological Society

February 1, 1975—Minnesota Club, St. Paul, Minnesota, 8:00 P.M.

The First K. W. Stenstrom Memorial Lecture to be given by: Leo G. Rigler, M.D., Professor and Chairman Emeritus, Department of Radiology, University of Minnesota and Professor of Radiology, Department of Radiological Sciences, University of California, Los Angeles.

"A Successful Academic Partnership: K. Wilhelm Stenstrom and the Department of Radiology of the University of Minnesota."

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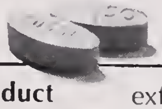

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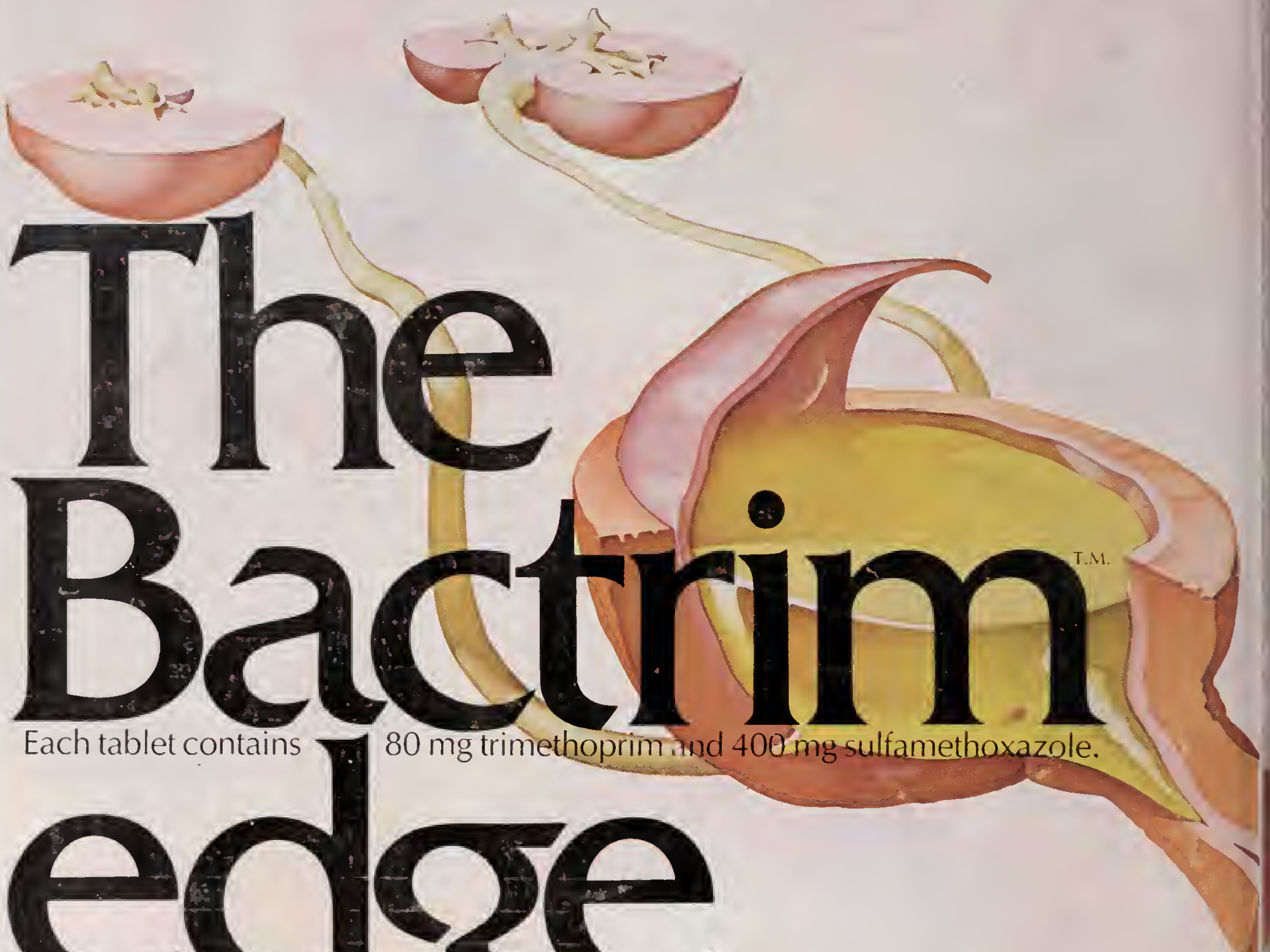

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ack Guy	New London

KITTSON COUNTY

oland Larter	Hallock

KOOCHICHING COUNTY

eorge M. Crow	International Falls
rederick H. Walter	International Falls

LAC QUI PARLE COUNTY

hester A. Anderson	Madison

LAKE COUNTY

. E. Church	Two Harbors
onald Haase	Silver Bay

LAKE-OF-THE-WOODS COUNTY

llen G. Janecky	Baudette

LE SUEUR COUNTY

E. Anderson	Le Sueur

LINCOLN COUNTY

eRoy Mueller	Hendricks
. D. Mulder	Ivanhoe

LYON COUNTY

. A. Peterson	Marshall
. M. Odland	Marshall

MAHNOMEN COUNTY

harles B. Mercil	Mahnomen

MARSHALL COUNTY

. A. Pinsonneault	Warren

MARTIN COUNTY

eorge N. Kraemer	Fairmont
. A. Williamson	Fairmont

McLEOD COUNTY

lark Truesdale	Glencoe
obert Hegrenes	Hutchinson
ohn J. Smyth	Lester Prairie

MEEKER COUNTY

redrick S. Schnell	Litchfield
. Olson	Litchfield
oseph C. Houts	Dassel

MILLE LACS COUNTY

. B. Metcalf	Princeton

MORRISON COUNTY

W. Watson	Little Falls
ilo Hansen	Little Falls
. J. Stein	Pierz

MOWER COUNTY

Harold J. Anderson	Austin
T. M. Seery	Austin
H. Miller	Austin
Clifford Pesonen	Austin

MURRAY COUNTY

R. F. Pierson	Slayton
J. L. Bader	Slayton
H. D. Patterson	Slayton
Dean Nywall	Slayton

NICOLLET COUNTY

Curtis Stolee	St. Peter

NOBLES COUNTY

M. W. Plucker	Worthington
B. C. Faul	Worthington
L. C. Strough	Worthington

NORMAN COUNTY

B. Kinkade	Ada

OLMSTED COUNTY

Stephen D. Mills	Rochester
James R. Doyle	Rochester
Theodore O. Wellner	Rochester
Deloran L. Thurber	Rochester
C. Michael Johnson	Rochester
Thomas J. Goodenow	Rochester
David R. Sanderson	Rochester

OTTER TAIL COUNTY

Roy Nelson	Fergus Falls
Homer Carlson	Pelican Rapids
C. W. Lewis	Henning
L. Syverson	Fergus Falls

PENNINGTON COUNTY

George Martin	Thief River Falls

PINE COUNTY

F. M. Mach	Pine City

PIPESTONE COUNTY

Jack W. Strand	Jasper
J. G. Lohmann	Pipestone
Roland Beckering	Edgerton

POLK COUNTY

Howard Wikoff	Crookston

POPE COUNTY

Gordon E. Lee	Glenwood
Berton A. Kolp	Glenwood
Foster D. Bucher	Starbuck

RAMSEY COUNTY

Ernest Hammes	St. Paul
John Frost	St. Paul
Henry Blumberg	St. Paul
John F. Perry	St. Paul
Charles McCafferty	St. Paul
Joseph L. Norquist	St. Paul
John Rauenhorst	St. Paul
Fred B. Wilson	St. Paul
Robert Powers	St. Paul
Robert S. Flom (ex officio)	St. Paul
Donald E. Roach (ex officio)	St. Paul

RED LAKE COUNTY

David Mersy	Red Lake Falls

REDWOOD COUNTY

James B. Flinn	Redwood Falls
G. W. Kaminski	Redwood Falls
G. E. Nelson	Redwood Falls

RENVILLE COUNTY

C. A. Anderson	Hector
Leo Furr	Bird Island

RICE COUNTY

Roy H. Good	Faribault
Asa Graham	Faribault
David Halvorson	Northfield
J. Gordon Beaton	Northfield

ROCK COUNTY

Darrel Siebert	Luverne
F. W. Bofenkamp	Luverne
D. M. Odland	Luverne

ROSEAU COUNTY

Jack Delmore	Roseau

ST. LOUIS COUNTY

W. J. Brooker	Duluth
C. D. Eklund	Duluth
W. H. Grohs	Duluth
G. E. Holt	Duluth
A. J. Jacklin	Duluth
H. H. Reed	Duluth
Bayard T. French	Hibbing
Kenneth E. Ahola	Hibbing
Robert Nelimark	Virginia
Richard R. Moyer	Hibbing
Wendell Engelstad	Virginia
David J. Richter	Virginia

SCOTT COUNTY

James Ponterio	Shakopee

SHERBURNE COUNTY

G. H. Tesch	Elk River

SIBLEY COUNTY

A. F. Dysterheft	Gaylord
John M. Vener	Arlington

STEARNS-BENTON COUNTY

G. K. Kvistberg	St. Cloud
C. D. Stiles	Foley
R. J. Salk	Albany
L. Stahn	St. Cloud
B. L. John	St. Cloud
J. J. Ballantine	St. Cloud

STEELE COUNTY

D. H. Dewey	Owatonna
F. C. Anderson	Owatonna
D. R. Halvorsen	Owatonna

STEVENS COUNTY

R. A. Rossberg	Mor
O. A. Eide	Hanco
Robert Watson	Mor

SWIFT COUNTY

Edward Kaufman	Applet
N. Wagner	Bens
T. S. Eberley	Bens

TODD COUNTY

David Howard	Long Prai
William Mennis	Stapl
Tim Schmitt	Browervi

TRAVERSE COUNTY

James R. Poole	Wheat
Joseph Pettko	Wheat

WABASHA COUNTY

B. J. Bouquet	Wabas
R. N. Bowers	Lake Ci
William P. Gjerde	Lake Ci
Gary Feigal	Lake Ci

WADENA COUNTY

Leland Reichelt	Wade
W. E. Parker	Sebe
W. B. Halme	Wade

WASECA COUNTY

Patrick Hergott	Wase
S. T. Normann	Wase

WASHINGTON COUNTY

G. T. Midboe	Forest La
Paul W. Nerothin	Forest La

WATONWAN COUNTY

R. A. Parsons	St. Jam
Herbert Boysen	Made

WILKIN COUNTY

L. O'Brien	Breckenrid
C. W. Jacobson	Breckenrid
Neil Kippen	Breckenrid

WINONA COUNTY

Herbert R. Heise	Wino
Robert B. Tweedy	Wino
Henry J. Roemer	Wino

WRIGHT COUNTY

R. Sandeen	Buff
Rok Shin	Howard La

YELLOW MEDICINE COUNTY

C. L. Lundell	Granite Fa
Darrell Carter	Granite Fa

Woman's Auxiliary to the Minnesota State Medical Association

1974-1975

Officers

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Irs. L. L. Bissinger	Seventh District	Brainerd
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inance—Mrs. Cyril R. Tifft ....St. Paul
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esolutions—Mrs. John Schotzko ....Blue Earth

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nternational Health—Mrs. Richard C. Tucker ......Edina
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Mrs. Robert F. Fischer ....St. Paul
WA/SAMA Liaison:
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Mrs. George Schaffhausen ....North Oaks
University of Minnesota—Duluth
Mrs. Robert E. Carter ....Duluth
Family Health—Mrs. W. G. Halverson ....Madelia
Community Health—Mrs. A. W. Diessner ....Afton
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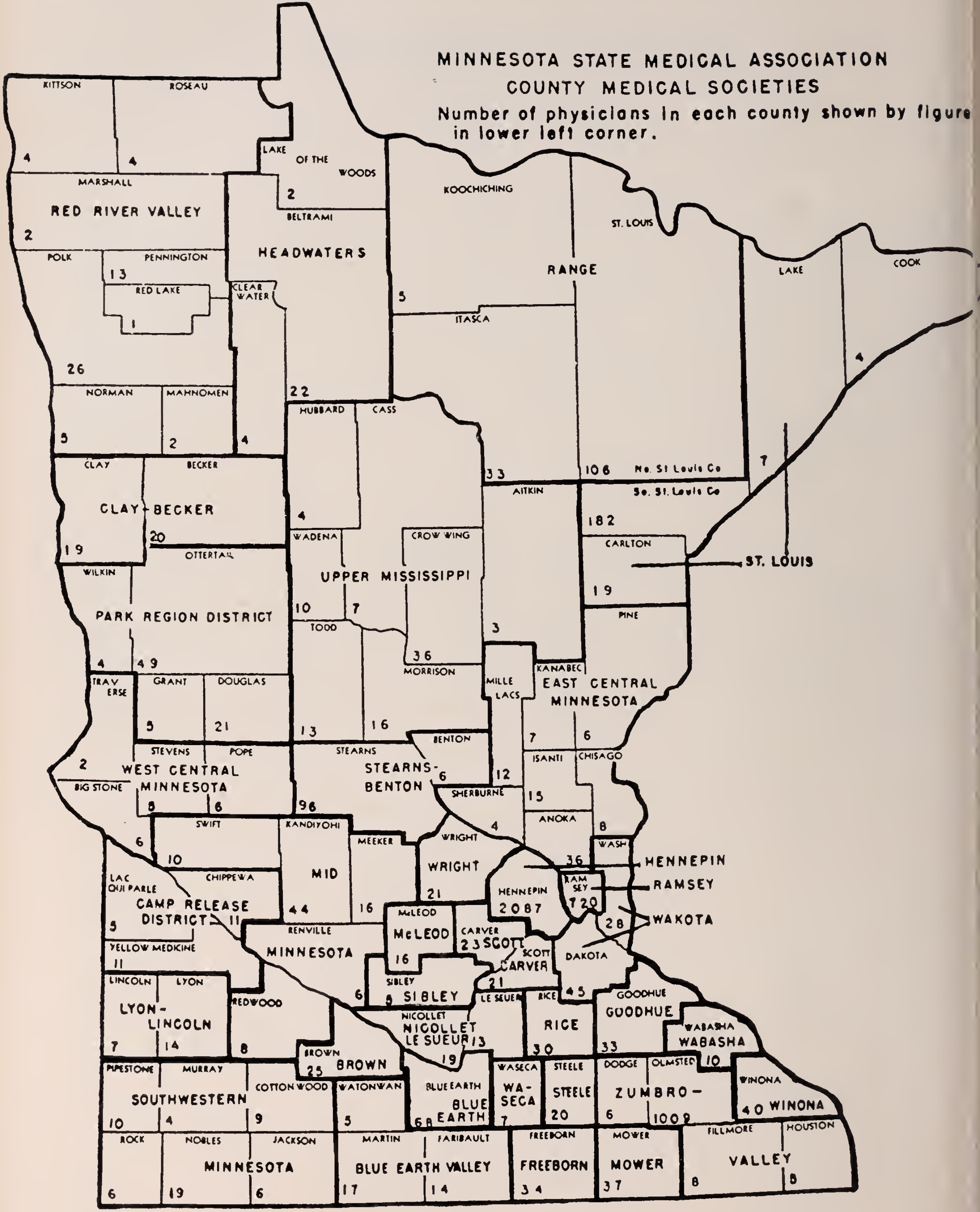

MINNESOTA STATE MEDICAL ASSOCIATION
COUNTY MEDICAL SOCIETIES
Number of physicians in each county shown by figure
in lower left corner.

KITTSON
4
ROSEAU
4
LAKE OF THE WOODS
2
MARSHALL
RED RIVER VALLEY
2
BELTRAMI
HEADWATERS
KOOCHICHING
ST. LOUIS
POLK
PENNINGTON
13
RED LAKE
1
CLEAR WATER
5
RANGE
LAKE
COOK
ITASCA
26
22
4
NORMAN
MAHNOMEN
5
2
4
HUBBARD
CASS
33
106
No. St Louis Co
7
So. St. Louis Co
CLAY
BECKER
AITKIN
CLAY-BECKER
182
4
20
19
WADENA
CROW WING
CARLTON
OTTERTAIL
ST. LOUIS
WILKIN
UPPER MISSISSIPPI
19
PARK REGION DISTRICT
10
7
PINE
TODD
3
36
4
49
MORRISON
KANABEC
TRAVERSE
GRANT
DOUGLAS
MILLE LACS
EAST CENTRAL MINNESOTA
5
21
13
16
7
6
BENTON
STEVENS
POPE
STEARNS
ISANTI
CHISAGO
2
WEST CENTRAL MINNESOTA
STEARNS-BENTON
6
12
BIG STONE
15
SHERBURNE
5
6
96
ANOKA
SWIFT
KANDIYOHI
4
8
6
MEEKER
WRIGHT
WASH
10
36
HENNEPIN
LAC QUI PARLE
CHIPPEWA
MID
WRIGHT
RAMSEY
RAMSEY
CAMP RELEASE DISTRICT
11
21
HENNEPIN
2087
720
5
44
16
McLEOD
28
WAKOTA
RENVILLE
McLEOD
CARVER
23
SCOTT
YELLOW MEDICINE
MINNESOTA
16
SCOTT CARVER
DAKOTA
11
SIBLEY
21
LINCOLN
LYON
6
8
SIBLEY
LE SUEUR
RICE
45
GOODHUE
LYON-LINCOLN
REDWOOD
NICOLLET
GOODHUE
NICOLLET LE SUEUR
13
RICE
WABASHA
WABASHA
7
14
8
BROWN
19
30
33
10
BROWN
25
PIPESTONE
MURRAY
WASECA
STEELE
DODGE
OLMSTED
COTTONWOOD
WATONWAN
BLUE EARTH
WA-SECA
STEELE
ZUMBRO-
WINONA
SOUTHWESTERN
BLUE EARTH
40
WINONA
10
4
9
5
68
7
20
6
1009
ROCK
NOBLES
JACKSON
MARTIN
FARIBAULT
FREEBORN
MOWER
FILLMORE
HOUSTON
MINNESOTA
BLUE EARTH VALLEY
FREEBORN
MOWER
VALLEY
6
19
6
17
14
34
37
8
8

County Medical Society Roster

KEY TO SYMBOLS AS FOLLOWS
* Deceased
† Associate or Life
£ Resident or Intern
§ Medical Student
# Service
¶ Affiliate or Honorary
‡ Wife is Member of Woman's Auxiliary

BLUE EARTH COUNTY MEDICAL SOCIETY

Blue Earth County
Regular meetings, last Monday of the month
Annual meeting, December
Number of members 64

PRESIDENT

Marso, John	Mankato

SECRETARY

Manahan, William	Mankato

‡	Anderson, Oscar D.	Mankato
‡	Arnesen, Paul M.	Mankato
	Barbarisi, Charles F.	Mankato
‡	Batdorf, B. N.	Mankato
‡	Brady, Charles H., Jr.	Mankato
	Brauer, Harry H.	Mankato
†	Butzer, John A.	Mankato
	Cadbury, Jane B.	Mankato
‡	Chalgren, William S.	Mankato
‡	Conley, Robert H.	Mankato
	Dobson, Mervin W.	Mankato
‡	Dover, James W.	Mankato
‡	Eckert, Joseph F.	Mankato
‡	Eggert, Delmer C.	Mankato
‡	Eisenbeis, C. F.	Mankato
‡	Elliott, J. W.	Mankato
‡	Eustermann, John J.	Mankato
‡	Florine, Martin C.	Madison Lake
‡	Fortier, R. G.	Mankato
†	Franchere, Frederick W.	Lake Crystal
‡	Freeman, Donald H.	Mankato
‡	Geurs, Benjamin R.	Mankato
‡	Gislason, Paul H.	Mankato
‡	Grande, David W.	Mankato
‡	Hammar, Lawrence M.	Mankato
	Hankerson, Robert G.	Mankato
‡	Heimark, John J.	Mankato
‡	Heller, Edgar E.	Mankato
†	Hoeper, Philip G.	Chestnut Hill, MA
	Huffington, Herb L.	Waterville
†	Huffington, Herbert L.	Brownsville, Texas
†‡	Jones, Orville H.	Mankato
‡	Kearney, R. Wynn	Mankato
†	Kemp, Alphonse F.	Mankato
‡	Knowles, William D.	Mankato
	Lester, John W.	Mapleton
‡	Lindblom, Alton E.	Mankato
‡	Lippmann, Elmer W., Jr.	Mankato
‡	Lund, J. Benjamin	Mankato
‡	McBride, Alexander M.	Mankato
‡	McGregor, Byron C.	Mankato
	Manahan, William D.	Mankato
‡	Marso, John L.	Mankato
‡	Mathews, Wallace E.	Mankato
‡	Meredith, Donald C.	Mankato
	Mickelson, John C.	Los Angeles, CA
*	Morgan, Hugh O.	Amboy
‡	Norris, J. C.	Mankato
‡	O'Byrne, Alvaro	Mankato
‡	Ohrt, D. K.	Mankato
‡	Penn, George E.	Mankato
‡	Roth, Frederick D.	Mankato
	Rozeboom, Paul E.	Mankato
‡	Sanford, Raymond A.	Mankato
‡	Scheidel, Alois M.	Mankato
‡	Schmitz, Anthony A.	Mankato
‡	Setzer, Hobert J., Jr.	Mankato
‡	Sjoding, J. Donald	Mankato
‡	Smith, Harry J.	Lake Crystal
‡	Snider, Howard R.	Mankato
†	Stillwell, Walter C.	Mankato
‡	Swenson, Donald B.	Mankato
*	Thiem, Chester E.	Mankato
†	Vezina, John C.	Mapleton
‡	Von Drasek, Joseph	Mankato
‡†	Wentworth, Albert J.	Mankato

BLUE EARTH VALLEY MEDICAL SOCIETY

Martin, Watonwan and Faribault Counties
Regular meetings, third Wednesday of each month
Annual meeting in November
Number of members 40

PRESIDENT
Marso, John .... Mankato
SECRETARY
Schotzko, J. R. .... Blue Earth
‡ Anderson, John W. .... Blue Earth
Armstrong, Ralph S. .... Winnebago
§ Bell, Clifford .... Blue Earth
‡ Bellomo, John .... Fairmont
†‡ Boysen, Herbert .... Madelia
Cox, Russell L. .... Estherville, IA
‡ Cullen, Robert M. .... Elmore
‡ Drexler, George W. .... Blue Earth
‡ Feigal, William M. .... Fairmont
‡ Gardner, Jack K. .... Fairmont
Halverson, D. E. .... Highland, CA
‡ Halverson, William G. .... Madelia
‡ Hanson, Lewis .... Frost
‡ Holstine, John D. .... Fairmont
Hruza, William J. .... Sioux Falls, SD
‡ Kraemer, George N. .... Fairmont
‡ Krause, Carl W. .... Fairmont
‡ Lester, Malcolm J., Jr. .... Truman
‡ Lindahl, Merlyn J. .... Sherburn
‡ Mijares, Wilfredo .... Fairmont
† Mills, John L. .... Winnebago
‡ Moulton, Keith B. .... St. James
‡ Nickerson, Neil D. .... Fairmont
‡ Parsons, R. A. .... St. James
Parsons, Ralph L. .... Trimont
‡ Pitcher, Arlo L. .... St. James
†‡ Russ, Homer H. .... Blue Earth
‡ Schotzko, John R. .... Blue Earth
Schulz, Robert W. .... Fairmont
‡ Sears, Martin F. .... Fairmont
‡ Tempel, J. W. .... Blue Earth
‡ Thayer, Ellsworth A. .... Fairmont
‡ Venugopal, M. .... Blue Earth
‡ Virnig, Mark P. .... Wells
‡ Virnig, Richard P. .... Wells
‡ Wandke, Otto E. .... Fairmont
‡ Watkins, John A. .... Wells
‡ Williamson, Harold A. .... Fairmont
†‡ Zemke, Erhart E. .... Fairmont
‡ Zemke, Robert L. .... Fairmont

BROWN COUNTY MEDICAL SOCIETY

Brown County
Regular meetings, second Tuesday
January, April, July and October
Annual meeting in January
Number of members 28

PRESIDENT
Kaiser, Milton .... New Ulm
SECRETARY
Vogel, Ann .... New Ulm
‡ Black, William A. .... New Ulm
‡ Boyle, Francis J. .... Springfield
‡ Burnett, Joseph W. .... New Ulm
‡ Cairns, Robert J. .... Redwood Falls
Carthey, Frank J. .... New Ulm
Fesenmaier, Otto B. .... Pasadena, CA
† Fritsche, Albert .... New Ulm
‡ Fritsche, Carl J. .... New Ulm
‡ Fritsche, Theodore R. .... New Ulm
‡ Galvin, Carroll .... Sleepy Eye
Gilles, Thomas F. .... Fairfax
‡ Johnson, Rex R. .... New Ulm
‡ Kaiser, Milton L. .... New Ulm
‡ Keithahn, Elmer E. .... Sleepy Eye
Keithahn, M. K. .... Lamberton
‡ Kitzberger, Peter J. .... New Ulm
Muesing, William J. .... New Ulm
† Nuessle, Walter G. .... Springfield
‡ Penk, Engward L. .... Springfield
† Peterson, Roy A. .... Vesta
‡ Rimas, Mathew J. .... Comfrey
Ringhofer, Lawrence .... New Ulm
‡ Saffert, Cornelius A. .... New Ulm
Vogel, Ann C. .... New Ulm
Vogel, Howard A. .... New Ulm
Wing, Elton G. .... Sleepy Eye
Wohlrabe, Donald E. .... Springfield
† Wohlrabe, Edwin J. .... Springfield

CAMP RELEASE DISTRICT MEDICAL SOCIETY

Chippewa, Lac qui Parle and Yellow Medicine Counties
Regular meetings, second Thursday of each month
except July and August
Annual meeting, December
Number of members 23

PRESIDENT
Carter, Kenneth R. .... Granite Falls
SECRETARY
Carter, Darrell L. .... Granite Falls
‡ Allen, John H. .... Montevideo
‡ Anderson, Chester A. .... Madison
‡ Birkey, Thomas G. .... Montevideo
‡ Boody, George J. .... Cambridge
‡ Borgerson, M. A. .... Hanley Falls
† Burns, Floyd M. .... Milan
‡ Camp, Ray J. .... Madison

Camp Release District Medical Society (Continued)

‡	Carter, Darrell L.	Granite Falls
‡	Carter, Kenneth R.	Granite Falls
	Coones, Michael	Montevideo
‡	Hagberg, Norman L.	Montevideo
†‡	Hauge, Malvin I.	Marcell
*‡	Johnson, Vilhelm M.	Dawson
¶	Jordan, Kathleen B. Smith	Granite Falls
‡	Kremer, Jerome L.	Montevideo
‡	Lima, Ludvig R.	Montevideo
‡	Lundell, Carl L.	Granite Falls
‡	Maus, Philip W.	Dawson
‡	Niazi, Suad A.	Granite Falls
‡	Owens, William A.	Montevideo
	Radke, Robert L.	Milan
	Roust, Henry A.	Montevideo
‡	Schmidt, Paul G.	Granite Falls
‡	Westby, Norval M.	Madison

CLAY-BECKER COUNTY MEDICAL SOCIETY

Clay and Becker Counties
Regular meeting, April
Annual meeting, November
Number of members 29

	PRESIDENT	
	Odland, M. E.	Detroit Lakes
	SECRETARY	
	Knapp, J. F.	Detroit Lakes
‡	Bigler, Earl E.	Perham
	Bigler, Ivan E.	Perham
	Bologna, Camillo V.	Moorhead
†	Bottolfson, B. T.	Moorhead
	Brenk, Paul E.	Detroit Lakes
	Carlon, Donald L.	Moorhead
‡	Carlson, Vernon J.	Moorhead
‡	Colliton, Patrick A.	Moorhead
‡	Covey, Kenneth W.	Moorhead
‡	Dodds, William C.	Detroit Lakes
‡	Duncan, James W.	Moorhead
	Groth, Mary K.	Moorhead
‡	Holten, John	Moorhead
†	Johnson, Olga H.	Moorhead
	Knapp, James F.	Detroit Lakes
	Lerud, M. Mark	Detroit Lakes
	Lorentzen, Ernest S.	Detroit Lakes
	March, Barrie L.	Detroit Lakes
	Mattson, Larry D.	Detroit Lakes
	Midthune, Andreen S.	Lake Park
	Nakamura, James Y.	Detroit Lakes
	Odland, Mark E.	Detroit Lakes
‡	Rice, Hagbart G.	Moorhead
‡	Rutledge, John B.	Detroit Lakes
*†	Rutledge. Lloyd H.	Detroit Lakes
	Saxman, Gertrude O.	Ulen
‡	Simison, Carl	Barnesville
‡	Thysell, Vernon D.	Moorhead
	Watson, Robert N.	Detroit Lakes
	Watson, Virgil A.	Detroit Lakes

EAST CENTRAL MINNESOTA MEDICAL SOCIETY

Chisago, Isanti, Kanabec, Mille Lacs,
Pine and Sherburne Counties
Regular meetings first Tuesday of even
months of the year except August
Annual meeting, first Tuesday in December
Number of members 40

	PRESIDENT	
	Erickson, Carlton	Chisago City
	SECRETARY	
	Seecamp, Carsten	Cambridge
ε	Aruguete, J.	Chicago, IL
*‡	Bartholdt, H. P.	Mora
‡	Berglund, Alvin E.	Cambridge
‡	Brettingen, Larry J.	Mora
	Bunker, Bevan W.	Anoka
‡	Burseth, Edgar C.	Mora
‡	Deason, Keith B.	Chisago City
‡	Erickson, Carlton	Chisago City
‡	Ericsson, Kermit C.	Cambridge
	Gailitis, Veronika M.	St. Paul
†	Grinvalds, Anna O.	St. Paul
‡	Hartzler, Paul L.	Cambridge
‡	Hovde, Gordon W.	Chisago City
	Huber, Robert W.	St. Croix Falls, WI
*	Hubin, Edwin G.	Sandstone
	Johnson, Aldridge F.	St. Paul
†	Kelsey, Carleton G.	St. Paul
‡	Lamusga, David J.	Cambridge
‡	Larson, Gerald E.	Cambridge
‡	Lindquist, Dale C.	Lindstrom
‡	Mach, Ralph F.	Pine City
‡	Magnuson, Raymond C.	Cambridge
	Metcalf, Norman	Princeton
‡	Murthy, K. V. K.	Mora
‡	Nordman, Willard F.	Mora
‡	Nygren, William T.	Braham
‡	Overgaard, Peter H.	Lindstrom
‡	Peterson, Alvin C.	Mora
‡	Pivac (Popivich) Dragojla	Milwaukee, WI
‡	Reiners, Gary	Cambridge
†	Roehlke, Arthur E.	Elk River
‡	Runquist, Richard	Cambridge
‡	Seecamp, Carsten H.	Cambridge
	Sommer, R. K.	Elk River
†	Spurzem, Raymond J.	Anoka
†‡	Stratte, Alf K.	Pine City
‡	Tesch, Gordon H.	Elk River
	Textor, Jerome D.	Champlin
‡	Travis, Richard C.	Elk River
‡	Wood, Ray	Cambridge
‡	Wicklund, Paul	Cambridge

FREEBORN COUNTY MEDICAL SOCIETY

Freeborn County
Regular meetings, third Thursday of even months
Annual meeting, December
Number of members 36

	PRESIDENT	
	Shepard, Richard	Albert Lea
	SECRETARY	
	Ellertson, Leonard M.	Albert Lea
‡	Barr, Lowell C.	Albert Lea
‡	Barr, Lowell W.	Albert Lea
‡	Blumer, Arlo R.	Albert Lea
‡	Buege, William	Albert Lea
†	Burns, Catherine	Excelsior
‡	Burns, James F.	Albert Lea
	Cole, George A.	Albert Lea
	Donovan, Daniel L.	New Brighton
‡	Egge, Sanford G.	Albert Lea
‡	Ellertson, Leonard M.	Albert Lea
‡	Erdal, Ove A.	Albert Lea
	Gamble, Elbert J.	Roseville
‡	Gill, Theodore M.	Albert Lea
‡	Halvorson, Harold C.	Albert Lea
‡	Hansen, Theodore M.	Albert Lea
‡	Karan, E. K.	Albert Lea
‡	Keil, Marcus A.	Albert Lea
‡	Menefee, Edward C.	Albert Lea
	Myers, Theodore P.	Albert Lea
‡	Neel, Harry B.	Albert Lea
	Nelson, Clayton E. J.	Albert Lea
‡	Nesheim, Martin O.	Albert Lea
†	Palmer, Clinton G.	Albert Lea
‡	Pogue, Charles G.	Albert Lea
‡	Rose, Cordt	Albert Lea
‡	Schmidt, Ruben F.	Alden
‡	Shepard, Richard	Albert Lea
‡	Sherman, Alfred G.	Albert Lea
	Steiner, Leon E.	Albert Lea
	Stoker, Lynn C.	Albert Lea
‡	Thompson, Thoburn F.	Albert Lea
=	Thorson, Steven J.	Bethesda, MD
‡	Treanor, Thomas A.	Albert Lea
†‡	Whitson, Sidney A.	Albert Lea
‡	Wilcox, G. Charles	Albert Lea
‡	Willie, James A.	Albert Lea

GOODHUE COUNTY MEDICAL SOCIETY

Goodhue County
Regular meeting, April and November
Annual meeting, November
Number of members 28

	PRESIDENT	
	Jackish, George E.	Red Wing
	SECRETARY	
	Schulenberg, Robert N.	Red Wing
‡	Akins, Willard M.	Red Wing
‡	Billings, Harry H.	Red Wing
*‡	Biltz, John F.	Red Wing
‡	Bruns, Donald L.	Red Wing
†‡	Brusegard, James F.	Red Wing
‡	Delahunty, John R.	Red Wing
	Falls, John L.	Red Wing
‡	Fauchald, Nils, Jr.	Red Wing
	Friedrich, Bradford E.	Red Wing
‡	Halvorson, James W.	Zumbrota
*‡	Hartnagel, Grant F.	Red Wing
‡	Hawley, George M. B.	Red Wing
‡	Jackish, George E.	Red Wing
‡	Juers, Edward H.	Red Wing
‡	Kuehner, Marvin E.	Red Wing
‡	Larson, Oliver E. H.	Zumbrota
	Leaf, Donn S.	Red Wing
†	Meyer, Frederick C.	Kenyon
‡	Molenaar, Robert E.	Cannon Falls
‡	Moshfeghi, Mohammad M.	Red Wing
‡	Nicolosi, Charles W.	Red Wing
	Rayner, Ralph R.	Red Wing
‡	Roth, Charles W.	Red Wing
‡	Sander, John L.	Red Wing
	Schroeder, Glenn E.	Red Wing
‡	Schulenberg, Robert N.	Red Wing
	Sherman, Royal V.	Red Wing
	Walter, William E.	Wanamingo
‡	Wasmund, Clarence W.	Red Wing
‡	Williams, Marland R.	Cannon Falls

HEADWATERS MEDICAL SOCIETY

Beltrami, Clearwater and Lake of the Woods Counties
Regular meetings to be determined
Annual meeting, 2nd Saturday in September
Number of members 30

	PRESIDENT	
	Reeber, Erick	Bagley
	SECRETARY	
	Gregoire, Earl	Bemidji
	Boysen, Alexander	Bemidji
‡	Brink, Adlai A.	Baudette
	Brown, James R.	Bemidji
	Deweese, Joel T.	Bemidji
	Deweese, Wilford J.	Bemidji
	Doebler, Myron I.	Bagley
‡	Franklin, Gordon W.	Northome
	Gregoire, Earl	Bemidji
	Griffin, John W.	Bemidji
	Hildebrand, John E.	Bemidji
‡	Janecky, Allen G.	Baudette
†	Johnson, Einer W.	Bemidji
	Laradie, Franklin A.	Bemidji
†	Larson, Leroy J.	Bagley
	Lundborg, Gary T.	Bemidji
	Lundsten, Leslie C.	Bemidji
	Martin, Frederick F.	Bagley
	Palmer, Harry A.	Blackduck
	Pearson, Harris L.	Bagley
	Reeber, Erick	Bagley
‡	Reid, Howard C.	Bemidji
‡	Roholt, Hartvig B.	Bemidji
	Slater, Edward C.	Bemidji
	Sondreal, Wesley D.	Bemidji
	Thompson, James R.	Bemidji
	Whittemore, Dexter D.	Bemidji
	Will, Theodore J.	Bemidji
‡	Wilson, Bruce C.	Bemidji
	Winkler, Gary L.	Bemidji
	Wohlfiel, Dwayne L.	Bemidji

HENNEPIN COUNTY MEDICAL SOCIETY

Hennepin County
Regular meetings, October, March, except when
otherwise designated
Annual meeting in October
Number of members 1573

PRESIDENT
Linderholm, Bruce E. ....Minneapolis
SECRETARY
Lund, George W. ....Minneapolis
EXECUTIVE SECRETARY
Hoban, Thomas W., Mr. ....Minneapolis

	Aadalen, Richard J.	Minneapolis
	Aamoth, Gordon M.	Minneapolis
	Abramson, Burton I.	Minneapolis
*	Abramson, Milton	Minneapolis
‡	Abullarade, Jose A.	Minneapolis
‡	Abuzzahab, Faruk S., Sr.	Minneapolis
	Adams, George L.	Minneapolis
‡	Adams, Richard I.	Minneaplois
‡	Adicoff, Arnold	Minneapolis
	Adkins, C. Douglas	Minneapolis
‡	Adkins, James T.	Coon Rapids
	Agee Andrew R.	Minneapolis
‡	Agustsson, Hreidar	Minneapolis
‡	Ahern, Eugene E.	Minneapolis
	Akbar, Sajady	Minneapolis
‡	Aksoy, Mustafa M.	Minneapolis
	Alari, Heino	Excelsior
§	Alexander, Gordon L.	Hopkins
†‡	Aling, Charles A.	Minneapolis
	Alkon, Ellen	Minneapolis
‡	Allen, James R.	Minneapolis
§	Alper, Richard E.	Minneapolis
	Alt, Thomas H.	Minneapolis
	Alter, Milton	Minneapolis
‡	Amatuzio, Donald S.	Minneapolis
‡	Amren, Don P.	Minneapolis
‡	Anderegg, Alfred F.	Minneapolis
	Andersen, James G.	Minneapolis
	Andersen, Robert C.	Minneapolis
‡	Anderson, Arnold S.	Minneapolis
§	Anderson, Darrel R.	Hopkins
	Anderson, David M.	Minneapolis
†	Anderson, Ernest R.	Minneapolis
‡	Anderson, Frank J.	Minneapolis
	Anderson, John A.	Minneapolis
	Anderson, John R.	Minneapolis
†‡	Anderson, Karl W.	Excelsior
‡	Anderson, Quentin N.	Minneapolis
	Anderson, Richard W.	Minneapolis
	Anderson, Roger E.	Minneapolis
	Anderson, Roger L.	Minneapolis
	Anderson, U. Schuyler	Minneapolis
	Anderson, Wallace E.	Minneapolis
‡	Anderson, William H.	Minneapolis
	Anderson, William T.	Minneapolis
	Andre, James C.	Minneapolis
†	Andreassen, Einar C.	Minneapolis
‡	Andreassen, Rolf L.	Minneapolis
‡	Andresen, Karl d'A	Minneapolis
‡	Ankner, Frank J.	Minneapolis
	Ansari, Azam	Minneapolis
	Anonsen, Richard E.	Minneapolis
	Anselment, Lois A.	Excelsior
	Arenson, Jeffrey A.	Minneapolis
	Arey, Stuart Lane	Minneapolis
‡	Arhelger, Stuart W.	Minneapolis
‡	Arlander, Clarence E.	Minneapolis
	Arlander, Thomas R.	Minneapolis
‡	Arling, Leonard S.	Minneapolis
	Arms, James J.	Minneapolis
	Armstrong, Byron H.	Minneapolis
	Arnar, Orn	Minneapolis
†	Arnold, Ann W.	Minneapolis
	Arnold, Thomas B.	Minneapolis
*	Aughenbaugh, John W.	Minneapolis
	Ausman, James I.	Minneapolis
‡	Avant, Robert F.	Minneapolis
	Ayala, Giovanni F.	Minneapolis
	Azad, Manouchehr	Minneapolis
	Azzam, Fouad G.	Minneapolis
	Bachmann, Sigrid A.	St. Paul
‡	Backus, Reno E.	Minneapolis
§	Baggenstoss, Gary A.	Minneapolis
‡	Baggenstoss, Osmond J.	Minneapolis
‡	Bagley, Russell W.	Minneapolis
	Baken, Melvin P., Jr.	Minneapolis
	Baker, Abe B.	Minneapolis
‡	Baker, C. Camak	Minneapolis
‡	Baker, Daniel R.	Minneapolis
‡	Baker, Lowell H.	Minneapolis
‡	Baker, Milton E.	Minneapolis
	Bakke, Arnold C.	Minneapolis
‡	Balcos, Emmanuel G.	Minneapolis
*‡†	Balkin, Samuel G.	Minneapolis
	Balkins, John W.	Minneapolis
‡	Balogh, Charles J.	Minneapolis
	Bandt, Calvin M.	Minneapolis
†	Bank, Harry E.	Minneapolis
	Banovetz, John D.	Minneapolis
‡	Barnett, Robert M.	Minneapolis
‡	Barno, Alex	Minneapolis
‡	Barr, Maxwell M.	Minneapolis
‡	Barrett, Patrick J.	Minneapolis
‡	Barron, Jesse J.	Minneapolis
†‡	Barron, Moses	Minneapolis
	Barry, George J.	Minneapolis
	Bart, Bruce J.	Minneapolis
	Baumgartner, C. John	Minneapolis
‡	Beach, Northrop	Minneapolis
‡	Beard, Archibald H., Jr.	Minneapolis
	Bearon, Arthur H.	Minneapolis
	Becklund, Roger W.	Minneapolis
	Beecher, Lee H.	Minneapolis
	Beeman, John A.	Minneapolis
	Beirstein, Samuel	Minneapolis
†	Beiswanger, Richard H.	Edina
	Bell, Donald C.	Minneapolis
	Bellville, Titus P.	Minneapolis
	Belzer, Meyer S.	Minneapolis
‡	Bendel, Richard P.	Minneapolis
	Bendel, William L., Jr.	Coon Rapids
	Benesh, Louis A.	Minneapolis
‡	Benjamin, Edwin G.	Minneapolis
‡	Benjamin, Harold G.	Minneapolis
	Benjamin, Richard D.	Minneapolis
‡	Benjamin, Robert B.	Minneapolis
	Bensman, Alan S.	Minneapolis
	Benson, Ellis S.	Minneapolis
	Bentz, Herman D.	Anoka
‡	Berestka, Stephen J.	Minneapolis
	Berg, Clinton C.	Excelsior

Continued on next page

Hennepin County Medical Society *(Continued)*

Berger, Alex G. .... Minneapolis
‡ Bergh, George S. .... Minneapolis
Bergh, Solveig M. .... Minneapolis
Berglund, Eldon B. .... Minneapolis
‡ Bergquist, James R. .... Minneapolis
Bergstrom, Ralph W., Jr. .... Maple Plain
Bergstrom, William J. .... Minneapolis
*† Berkwitz, Nathaniel J. .... Minneapolis
Berman, David A. .... Minneapolis
Berman, Reuben .... Minneapolis
Bernstein, Dorothy M. .... Minneapolis
Bernstein, Irving C. .... Minneapolis
Berris, Harold .... Minneapolis
£ Berry. Douglas G. .... Minneapolis
Berry, Ronald N. .... Minneapolis
‡ Berzins, Rainis .... Minneapolis
†‡ Bessesen, Alfred N. .... Minneapolis
‡ Bevis, William D. .... Minneapolis
Bhatnagar, Prabha .... Plymouth
§ Biebl, Jonathan H. .... Richfield
Bieger, R. Cyril .... Minneapolis
Biery, M. Barbara .... Minneapolis
† Bieter, Raymond N. .... St. Paul
‡ Bilgutay, Aydin M. .... Minneapolis
Bilka, Paul J. .... Minneapolis
Billman, Herbert R. .... Minneapolis
Binder, Manuel R. .... Minneapolis
Bingham, George C. .... Pensacola, FL
†‡ Bishop, James R. .... Minnetonka
Bittick, Wilbur H. .... Minneapolis
‡ Blackard, Clyde E. .... Minneapolis
‡ Blake, Allan J. .... Hopkins
§ Blake, David P. .... Hopkins
‡ Blake, James A. .... Hopkins
‡ Blake, Paul S. .... Minneapolis
Bland, Charles S. .... Minneapolis
‡ Bloedel, Traugott J. .... Osseo
‡ Blomberg, Robert D. .... Minneapolis
‡ Bloom, David .... Minneapolis
Bloom, Norman B. .... Minneapolis
Blum, Paul M. .... Minneapolis
‡ Blumenthal, Malcolm N. .... Minneapolis
‡ Boardman, Peter J. .... Wayzata
Boardman, William J. .... Minneapolis
Bocklage, Joseph F. .... Minneapolis
Bofenkamp, Benjamin .... Minneapolis
†‡ Boies, Lawrence R., Sr. .... Hopkins
Boller, M. A. .... Minneapolis
£ Bolt, Donald A. .... Ft. Lauderdale, FL
‡ Bonewell, George W. .... Minneapolis
† Borman, Chauncey N. .... Minneapolis
Boros, Stephen J. .... Minneapolis
Borowicz, Leonard A. .... Minneapolis
Borrud, Chester C. .... Anoka
Bouthilet, Florence J. .... St. Paul
† Bowers, Gordon G. .... Excelsior
‡ Bowlin, Paul F. .... Minneapolis
† Boynton, Ruth E. .... Miami, FL
Boyum, Allan J. .... Minneapolis
‡ Bradford, David S. .... Minneapolis
Bradley, Jeanne B. .... Minneapolis
Bradley, John G. .... Minneapolis
‡ Bradley, William E. .... Minneapolis
Brage, John R. .... Minneapolis
Brakke, Mark A. .... Coon Rapids
‡ Brandt, Henry E. .... Minneapolis
‡ Bransford, Paul W. .... Minneapolis
‡ Brauer, William W. .... Minneapolis
‡ Braun, Rene .... Minneapolis
‡ Breitenbucher, Robert B. .... Minneapolis
†‡ Brekke, Harvey J. .... Minneapolis
‡ Brennan, Joseph G. .... Minneapolis
Brill, Alice K. .... Bloomington
Briones, Bienvenido R. .... Hopkins
Brodsky, Ivan L. .... Minneapolis
‡ Bromer, Michael D. .... Minneapolis
*† Brooks, Charles N. .... Wayzata
Brown, David M. .... Minneapolis
‡ Brown, John H. .... Minneapolis
‡ Brown, William D., Jr. .... Minneapolis
‡ Brownfield, James A. .... Minneapolis
‡ Buchstein, Harold F. .... Minneapolis
Buchwald, James A. .... Minneapolis
‡ Buckley, Joseph J. .... Minneapolis
‡ Bugby, Robert D. .... Minneapolis
‡ Bugenstein, Robert H. .... Minneapolis
‡ Buie, Louis A., Jr. .... Minneapolis
Bundt, Robert E. .... Minneapolis
Buran, David J. .... Minneapolis
‡ Burchell, Howard G. .... Minneapolis
Burkholder, Dayton D. .... Anoka
‡ Burman, Richard E. .... Minneapolis
‡ Burnham, Wesley H. .... Minneapolis
Burton, Thomas P. .... Minneapolis
†‡ Cable, Morris L. .... Minneapolis
† Cabot, Clyde M. .... Ft. Lauderdale, FL
§ Caldwell, Frank .... Minneapolis
‡ Calin, S. Hartley .... Minneapolis
Cameron, Bruce P. .... Minneapolis
*† Cameron, Isabell L. .... Minneapolis
‡ Campbell, Denis V. .... Minneapolis
Campbell, Marilyn R. M. .... Minneapolis
† Campbell, Orwood J. .... Tucson, AZ
Campbell, Ronald G. .... Minneapolis
‡ Card, William H. .... Minneapolis
Cardle, James G. .... Minneapolis
‡ Cardle, John B. .... Minneapolis
‡ Carlander, Lester W. .... Minneapolis
Carlson, Charles V. .... Mound
Carlson, Clifford .... Minneapolis
‡ Carlson, Curtis H. .... Minneapolis
‡ Carlson, David J. .... Minneapolis
†‡ Carlson, Lawrence .... Minneapolis
£ Carlson, Pamela N. .... Minneapolis
£ Carlson, Richard W. .... Minneapolis
Carr, William J. .... Minneapolis
‡ Carrier, Thomas C. .... Minneapolis
‡ Caspers, Carl G. .... Minneapolis
‡ Cauble, Charles F. .... Minneapolis
‡ Cava, Eugenio A. .... Fridley
†‡ Cavanor, Frank T. .... Minneapolis
‡ Cavert, H. Mead .... Minneapolis
Cedarleaf, Shirley J. .... Edina
‡ Ceder, Elmer T. .... Minneapolis
Cella, Joseph A. .... Minneapolis
‡ Chadbourn, Wayne A. .... Minneapolis
Challman, S. Alan .... Minneapolis
Chally, Cecil H. .... Minneapolis
‡ Chandler, William M. .... Minneapolis
‡ Chedister, Charles R. .... Minneapolis
Chervenak, William A. .... St. Paul
‡ Chesler, Merrill D. .... Minneapolis
Child, Sherman B. .... Minneapolis
‡ Chisholm, Tague C. .... Minneapolis
Chizek, David J. .... Minneapolis
Chou, Shelley N. .... Minneapolis
‡ Christensen, Llewellyn E. .... Minneapolis

Hennepin County Medical Society *(Continued)*

	Christenson, Leland R.	Minneapolis
	Christgau, Roger A.	Minneapolis
	Christian, William L.	Minneapolis
	Cich, John A.	Minneapolis
£	Cintora, Ismar	Minneapolis
‡	Clark, Malcolm D.	Minneapolis
	Clark, Robert S.	Minneapolis
	Clay, Lyman B.	Minneapolis
‡	Cline, David W.	Minneapolis
	Cochrane, Ray F.	Minneapolis
	Coe, John I.	Minneapolis
	Cohan, Richard C.	Minneapolis
‡	Cohen, Bernard A.	Minneapolis
	Cohen, Ephraim B.	Minneapolis
‡	Cohen, Henry W.	Wayzata
*†	Cohen, Sumner S.	Minneapolis
	Coifman, Robert	Minneapolis
‡	Cole, James S.	Minneapolis
	Collinge, James A.	Minneapolis
‡	Conlon, Daniel C.	Minneapolis
‡	Cooper, John P.	Minneapolis
‡	Cooper, Robert R.	Minneapolis
†	Corniea, Albert D.	Minneapolis
	Correa, Dale H.	Minneapolis
	Corson, Wilfred A.	Minneapolis
‡	Cortez, Daniel P.	Minneapolis
‡	Coulter, Harold E.	Minneapolis
	Cowan, Donald W.	Minneapolis
	Craig, M. Elizabeth	Minneapolis
†‡	Cranmer, Richard R.	Laguna Hills, CA
†	Cranston, Robert W.	Minneapolis
‡	Creevy, Charles D.	Minneapolis
£	Creme, Joseph J.	Minneapolis
	Croissant, Raymond C.	Minneapolis
‡	Crowley, Leonard V.	Minneapolis
§	Cruz, Baltasar	St. Paul
	Cruz, Waldemar F.	Minneapolis
‡	Cullado, Andrionico F.	Minneapolis
	Culligan, Leo C.	Minneapolis
‡	Cundy, Donald T.	Minneapolis
‡	Curran, John P.	Minneapolis
	Cushing. Richard T.	Minneapolis
†	Cutts, George	Minneapolis
‡	Daggett, Donald R.	Minneapolis
*	Dahl, James C.	Minneapolis
†	Dahl, John A.	Minneapolis
	Dahlstrom, Donald D.	Minneapolis
†	Daniel, Donald H.	Wayzata
	Daniels, Clarke G.	Minneapolis
‡	Danoff, David	Minneapolis
‡	Danyluk, Michael	Minneapolis
	Dargay, Cyril P.	Minneapolis
‡	Daumann, Roy E.	Minneapolis
	David, Reuben	Hopkins
	Davis, Curtis E.	Minneapolis
‡	Davis, Michael W.	Minneapolis
	Davis, Thomas H.	Minneapolis
	Dawson W. John, Jr.	Minneapolis
	Deaton, Burrell H.	Minneapolis
	DeCasare, Ronald E.	Edina
	Dedeker, Kenneth L.	Wayzata
	De Haan, Eddie D.	Minneapolis
	Delzell, Allen W.	Minneapolis
‡	Diamond, Robert A.	Minneapolis
	Dickman, Roy W.	Minneapolis
	Diego, Benito B.	Fridley
*†	Diehl, Harold S.	New York, NY
	Diehl, James J.	Minneapolis
‡	Dierker, Heinrich A.	Minneapolis
	Dimants, Janis, Jr.	Minneapolis
‡	Doan, Robert E.	Wayzata
	Docherty, John A.	Minneapolis
‡	Donatelle, Edward P.	Grand Forks, ND
†	Dorge, Richard	Minneapolis
	Dornbach, Robert A.	Minneapolis
‡	Dorsey, George C., Jr.	Minneapolis
‡	Dorsey, William E.	Minneapolis
	Doscherholmen, Alfred	Minneapolis
‡	Dougan, Jerome W.	Minneapolis
	Doughman, Donald J.	Minneapolis
	doVale, Joao M.	Edina
†	Doxey, Gilbert L.	Minneapolis
§	Doyne, Holly L.	Minneapolis
‡	Drage, Charles W.	Minneapolis
‡	Dredge, Thomas E., Sr.	Minneapolis
‡	Drill, Frederick E.	Minneapolis
‡	Drill, Herman E.	Hopkins
	Dummer, Donald J.	Minneapolis
	Dumonceaux, Roland G.	Minneapolis
	Duncan, Donald A.	Minneapolis
	Dunkel, Thomas B.	Minneapolis
	Dunlap, David J.	Minneapolis
†‡	Dunlap, Earl H.	Minneapolis
‡	Dupont, Joseph A.	Excelsior
†	Duryea, Willis M.	Minneapolis
	Duryea, Willis M., Jr.	Minneapolis
†‡	Dvorak, Benjamin A.	Minneapolis
†	Dworsky, Samuel D.	Edina
	Earl, Stephan H.	Minneapolis
	Ebert, Richard V.	Minneapolis
	Eckerly, Jean R.	Minneapolis
‡	Eder, Walter P.	Minneapolis
	Edmondson, Hugh A., Jr.	Minneapolis
‡	Efteland, Myles E.	Minneapolis
	Ehrlich, S. Paul	Minneapolis
†	Eich, Matthew A.	Minneapolis
	Eichenlaub, John E.	Minneapolis
‡	Eichhorn, Edmund P., Jr.	Minneapolis
£	Eichten, John G.	Minneapolis
‡	Eifrig, David E.	Minneapolis
	Einzig, Mitchell J.	Wayzata
	Eisenberg, M. Michael	Minneapolis
‡	Eisenstadt, William S.	Minneapolis
†	Eitel, George D.	Minneapolis
	Ellingson, Richard B.	Minneapolis
	Ellington, Anna L.	Minneapolis
‡	Ellis, Cassius M. C., III	Minneapolis
‡	Ellis, John C., Jr.	Minneapolis
‡	Ellison, Evan S.	Minneapolis
	Elwood, Paul M., Jr.	Minneapolis
†	Emond, Joseph S.	Farmington
	Emond, Joseph S., Jr.	Farmington
‡	Engel, Joseph P.	Minneapolis
‡	Engel, William L.	Minneapolis
‡	Englund, Elvin F.	Minneapolis
‡	Engstrom, E. Duane	Minneapolis
‡	Engwall, Richard L.	Minnetonka
	Erickson, Jeffrey L.	Minneapolis
‡	Erickson, Laurence F.	Minneapolis
‡	Erickson, Myron E.	Minneapolis
‡	Ericson, John E.	Minneapolis
‡	Eselius, Erik P.	Minneapolis
‡	Esensten, Sidney	Minneapolis
	Etzwiler. Donnell D.	Minneapolis
‡	Eusebio, Ernesto	Minneapolis

(Continued on next page)

Hennepin County Medical Society *(Continued)*

†‡	Evans, Edward T.	Minneapolis
‡	Everhart, Clarence E., Jr.	Minneapolis
	Everly, Stephan S.	Minneapolis
£	Ewing, James W.	Bloomington
	Fallon, Virgil T.	Minneapolis
	Fangman, John J.	Minneapolis
	Farb, Harry F.	Minneapolis
	Farber Abigail F.	Minneapolis
	Farber, Roger E.	Minneapolis
‡	Farber, Lawrence A.	Minneapolis
	Farley, Harrison H.	Minneapolis
	Farrell, T. Edwin	Minneapolis
‡	Fehr, Peter E.	Minneapolis
	Feinberg, Philip	Minneapolis
	Feinberg, Samuel B.	Minneapolis
	Fernandez, Carlos H.	Minneapolis
‡	Fernandez, Rafael F., Jr.	Minneapolis
‡	Fetzek, Albert D.	Minneapolis
‡	Field, Charles	Hopkins
	Fifer, Ellen Z.	Minneapolis
	Fifer, William R.	Minneapolis
	Filiatrault, L. J.	Minneapolis
	Filipovich, Orest N.	Minneapolis
‡	Fingerman, David L.	Minneapolis
†‡	Fink, Leo W.	Minneapolis
‡	Fink, Robert J.	Edina
‡	Finkelstein, Joel	Minneapolis
‡	Finstad, James E.	Minneapolis
	Fisher, Don H.	Minneapolis
	Fisher, Howard W.	Minneapolis
‡	Fisher, Isadore	Minneapolis
§	Fleischer, Thomas A.	Minneapolis
	Fleming, Dean S.	Minneapolis
‡	Fliehr, Richard R.	Minneapolis
	Flora, George C.	Minneapolis
	Florence, David W.	Minneapolis
	Flory, W. Daniel	Minneapolis
	Foker, Leslie W.	Minneapolis
	Foley, Robert R.	Hopkins
‡	Foley, William A.	Minneapolis
‡	Folsom, Louis B.	Minneapolis
	Forbes, Edward F.	Minneapolis
†	Ford, W. Harold	Hopkins
	Fortuny, Ignacio E.	Minneapolis
	Foss, Donald L.	Minneapolis
§	Foster, Craig A.	St. Louis Park
‡	Foster, Orley W.	Minneapolis
	Fox, Donald P.	Minneapolis
‡	Fox, James Rogers	Edina
‡	Fraley, Elwin E.	Minneapolis
‡	Frane, Donald B.	Minneapolis
‡	Frane, Gerald T.	Minneapolis
‡	Fredlund, Jon S.	Anoka
‡	Freeman, Craig W.	Minneapolis
	Freeman, Donald W.	Minneapolis
	French, Lyle A.	Minneapolis
‡	Frey, Richard J.	Minneapolis
	Friberg, Joseph B.	Minneapolis
	Fried, Louis A.	Minneapolis
†	Friedell, Aaron	Minneapolis
	Friedell, George	Minneapolis
‡	Friedman, Harry S.	Minneapolis
‡	Friend, Charles A.	Minneapolis
‡	Fromke, Vincent L.	Minneapolis
	Frost, John B.	Minneapolis
	Fruchtman, Stanley A.	Minneapolis
‡	Frys, Russell N.	Minneapolis
	Fuglestad, Edson V.	Minneapolis
‡	Fuglestad, J. Roald	Minneapolis
†	Fuller, Alice H.	Minneapolis
†‡	Funk, Victor K.	Hopkins
	Furman, Christine	Minneapolis
	Gaard, Richard C.	Robbinsdale
‡	Gage, James R.	Minneapolis
‡	Galbraith, Richard F.	Minneapolis
	Gallagher, Larry J.	Mound
‡	Gallett, Lester E.	Minneapolis
†	Galligan, Margaret Mary D.	Minneapolis
	Galway, Charles F.	Minneapolis
	Gamble, William G.	Minneapolis
‡	Gannon, Paul G.	Minneapolis
	Garcia, Oscar	Coon Rapids
	Garamella, Joseph J.	Minneapolis
	Garetz, Floyd K.	Minneapolis
‡	Garske, George L.	Minneapolis
	Garten, Joseph L.	Minneapolis
‡	Garvey, James T.	Minneapolis
‡	Garvis, Gary E.	Minneapolis
	Gasik, Joseph M.	Minneapolis
£	Gauger, David W.	Edina
‡	Gault, N. L., Jr.	Minneapolis
	Gaviser, David	Minneapolis
	Geis, LeRoy F.	Minneapolis
	Geller, Joseph	Minneapolis
	Gendron, Joseph L.	Minneapolis
‡	Gentry, William C., Jr.	Minneapolis
	Gensberg, James P.	Minneapolis
	George, Vane P., Jr.	Le Sueur
	Gerster, Paul W.	Anoka
	Gesundheit, Sim	Minneapolis
	Gibbs, Robert W.	Minneapolis
‡	Giebenhain, John N.	Minneapolis
†‡	Giere, Joseph C.	Minneapolis
†	Giere, Richard W.	Edina
	Gilbert, Maurice G.	Minneapolis
	Gilbertsen, A. Sigrid	Minneapolis
	Gilbertsen, Victor A.	Minneapolis
£	Gilbertson, Gary F.	Bloomington
	Gilles, Paul J.	Minneapolis
‡	Gillund, T. Dean	Minneapolis
†	Gingold, Benjamin A.	Minneapolis
	Ginsberg, James P.	Minneapolis
	Glaeser, John H.	Minneapolis
	Godfrey, H. Wilson	Minneapolis
‡	Goehl, Reinhold O., Jr.	Minneapolis
	Goetz, Frederick	Minneapolis
	Gokcen, Barbara W.	Minneapolis
	Gokcen, Muharrem	Minneapolis
†	Goldberg, Isadore M.	Minneapolis
	Goldberg, Marvin E.	Minneapolis
‡	Goldberg, Stanley M.	Minneapolis
	Goldfarb, Benjie L.	Minneapolis
	Goldfarb, Mace G.	Minneapolis
†	Goldman, Theodore I.	Minneapolis
‡	Goldner, Meyer Z.	Minneapolis
	Goldstein, Alan L.	Hopkins
	Goltz, Robert W.	Minneapolis
‡	Good, Gary	Minneapolis
	Goodale, Robert L., Jr.	Minneapolis
	Goodchild, William R.	Minneapolis
	Gordon, John R.	Minneapolis
‡	Gordon, Sewell S.	Minneapolis
	Gorman, Jeffrey D.	Minneapolis
‡	Gozum, Ekrem	Minneapolis
	Grados, Carlos	Coon Rapids
	Grage, Theodor	Minneapolis
	Graham, John J.	Minneapolis
	Granquist, Richard D.	Minneapolis

Hennepin County Medical Society *(Continued)*

‡	Grant, James B.	Minneapolis
	Grant, Suzanne	Minneapolis
†	Gray, Royal C.	Minneapolis
#	Greden, John F.	Wheaton, MD
	Green, Clayton R.	Excelsior
	Green, Robert A.	Minneapolis
	Greenberg, Albert J.	Minneapolis
	Greene, Leonard H.	Minneapolis
	Greenfield, Irving	Minneapolis
¶	Greisheimer, Esther M.	Wayne, PA
£	Grenier, Stephen R.	Minneapolis
†	Grimes, Marian	Minneapolis
	Grimm, Roger	Minneapolis
	Grimmell, Francis J.	Minneapolis
	Grossling, Higinia C.	Minneapolis
	Grossling, Sergio F.	Minneapolis
	Grube, David W.	Minneapolis
‡	Gruys, Robert I.	Edina
‡	Guerrero, Rafael A.	Minneapolis
	Gullickson, Glenn, Jr.	Minneapolis
‡	Gunlaugson, Frederick G.	Minneapolis
‡	Gustafson, Paul O.	Minneapolis
‡	Gustafson, Robert W.	Mound
‡	Gustason, Harold T.	Minneapolis
‡	Gustilo, Ramon B.	Minneapolis
‡	Gutenkauf, Joseph J.	St. Paul
	Haas, John W.	Minneapolis
‡	Haberle, Charles A.	Minneapolis
	Haddad, Nick J.	Minneapolis
‡	Hagen, Kristofer	Minneapolis
‡	Hagen, Wayne S.	Minneapolis
‡	Haglin, John J.	Minneapolis
‡	Hakim, Ali A.	Minneapolis
‡	Hall, Arthur M.	Minneapolis
	Hall, Fredric C.	Minneapolis
‡	Hall, Harry B.	Minneapolis
‡	Hall, Loren J.	Minneapolis
‡	Hall, Wendell H.	Minneapolis
	Hambidge, Gove, Jr.	Minneapolis
	Hamel, Arnold L.	Minneapolis
‡	Hamel, Joseph I.	Minneapolis
	Hammerstrom, Robert N.	Minneapolis
‡	Handler, Seymour	Minneapolis
‡	Hanisch, Edward C., Jr.	Minneapolis
†‡	Hansen, Cyrus O.	Minneapolis
†	Hansen, Olga S.	Minneapolis
‡	Hansen, Rollin M.	Minneapolis
‡	Hanske, Edward A.	Minneapolis
	Hanson, A. Stuart	Minneapolis
†	Hanson, Harlow J.	Minneapolis
†	Hanson, Harold B.	Burnsville
‡	Hanson, Harold W.	Minneapolis
‡	Hanson, Mark C. L.	Minneapolis
	Hanson, Mildred S.	Minneapolis
‡	Hanson, Stephen L.	Minneapolis
*†	Hanson, William A. H.	Minnetonka
†	Hanson, William B.	Minneapolis
	Harkness, John W.	Minneapolis
£	Harris, James D.	Minneapolis
	Harris, Leon D.	Bloomington
†	Harrison, William C.	Minneapolis
	Hart, Terril H.	Wayzata
‡	Hartig, Paul R.	Minneapolis
†	Hartman, Evelyn E.	Minneapolis
	Hartman, Gene R.	Minneapolis
‡	Hartwig, John A.	Minneapolis
	Harty, Jerome L.	Fridley
	Harvey, Clyde B.	Ruleville, MS
‡	Hass, Frederick M.	Minneapolis
‡	Hastings, Donald W.	Minneapolis
‡	Hauge, Erling T.	Minneapolis
‡	Haugen, George W.	Minneapolis
	Haugen, John A.	Minneapolis
‡	Hauser, Donald C.	Minneapolis
‡	Hausman, William	Minneapolis
	Havel, Robert J.	Minneapolis
‡	Haven, Walter K.	Minneapolis
†	Hawkinson, Raymond P.	Minneapolis
‡	Hay, Lyle J.	Minneapolis
‡	Haywa, E. William	Minneapolis
‡	Hebbel, Robert	Minneapolis
‡	Hedrick, William L.	Minneapolis
‡	Heinz, John N.	Minneapolis
#	Heithoff, Kenneth B.	Bethesda, MD
	Heller, Ben I.	Minneapolis
	Heller, Steven A.	Minneapolis
	Helseth, Hovald K. Jr.	Minneapolis
‡	Hempel, Dean J.	Minneapolis
‡	Henrikson, Earl C.	Minneapolis
†	Herbert, Willis L.	Minneapolis
	Hernandez, Hermenegildo, Jr.	Minneapolis
‡	Hess, Carroll N.	Minneapolis
	Hess, Sheldon	Minneapolis
	Hetzler, John A.	Minneapolis
‡	Heupel, Hermann W.	Minneapolis
‡	Hewitt, Marshall I.	Minneapolis
	Hiatt, John A.	Minneapolis
	Hickok, David F.	Minneapolis
	Hiduchenko, Katherine	Minneapolis
‡	Hildebrandt, Walter C.	Minneapolis
‡	Hilgedick, William R.	Minneapolis
	Hilgermann, George O.	Minneapolis
£	Hill, David E.	Minneapolis
‡	Hill, David L.	Minneapolis
‡	Hill, Earl	Minneapolis
‡	Hill, Elmer M.	Minneapolis
£	Hill, John J.	St. Paul
‡	Hiller, Bruce H.	Minneapolis
‡	Hitchcock, Claude R.	Minneapolis
‡	Hodges, Kenneth V.	Minneapolis
	Hoekstra, Ronald E.	Minneapolis
†	Hoffert, Henry E.	Minneapolis
‡	Hoffman, Neil R.	Minneapolis
†	Hoffman, Roy A.	Minneapolis
‡	Hoffman, Walter Lees	Minneapolis
‡	Hofmann, Gerald N.	Minneapolis
‡	Holm, Donald F.	Minneapolis
‡	Holmberg, Conrad J.	Minneapolis
	Holmes, H. Spencer	Minneapolis
	Holt, Douglas	Minneapolis
	Holzapfel, Fred C.	Minneapolis
‡	Hopperstad, J. Jerome	Minneapolis
‡	Hoppes, Emerson E.	Minneapolis
‡	Horecki, Henry	Minneapolis
	Horns, Howard L.	Minneapolis
‡	Horns, Norman	Minneapolis
‡	Horns, Richard C.	Minneapolis
	Horowitz, Arthur J.	Minneapolis
	Horowitz, Marcel I.	Minneapolis
‡	Hoseth, Wayne L.	Minneapolis
	Hosfield, William B.	Minneapolis
	Hosteller, James P.	Minneapolis
‡	House, James H.	Minneapolis
	House, Roy F., Jr.	Minneapolis
‡	Householder, James R.	Minneapolis
	Hovland, Melvin L.	Wayzata

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Hennepin County Medical Society *(Continued)*
‡ Hovland, Richard D. ....Minneapolis
£ Howard, Richard J. ....Edina
Howard, Robert B. ....Minneapolis
Howard, Solomon E. ....Minneapolis
‡ Howell, Carter W. ....Minneapolis
‡ Howell, John L. ....Minneapolis
‡ Hoyt, C. Sherman ....Minneapolis
‡ Huff, John S. ....Minneapolis
‡ Hulteng, Donald B. ....Fridley
Hung, Jui-Sung ....Minneapolis
‡ Hurr, Maland C. ....Minneapolis
‡ Hustad, Edward G. ....Minneapolis
‡ Hymes, Alan C. ....Minneapolis
† Hymes, Charles ....Minneapolis
‡ Idstrom, Linneus G. ....Minneapolis
Ide, Arthur W., Jr. ....Minneapolis
‡ Indeck, Walter ....Minneapolis
Ingalls, Edgar G. ....Minneapolis
Iverson, Eleanor B. ....Minneapolis
‡ Iverson, Rolf M. ....Minneapolis
‡ Jackson, J. Albert ....Minneapolis
Jackson, Richard L. ....Minneapolis
‡ Jacobson, Leslie W. ....Minneapolis
Jacobson, Loren J. ....Minneapolis
Jacobson, Wyman E. ....St. Louis Park
‡ Jacoby, John S. ....Minneapolis
Jaffee, Manuel O. ....Minneapolis
‡ Janda, George W. ....Minneapolis
Janes, Alec L. ....Minneapolis
Jay, Alan R. ....Temple, TX
‡ Jefferies, William L. ....Minneapolis
‡ Jensen, Nathan K. ....Minneapolis
‡ Jensen, Paul A. ....Minneapolis
Jensen, Reynold A. ....St. Cloud
Jerome, Bourne ....Minneapolis
Jerome, Elizabeth B. K. ....Minneapolis
‡ Jeub, Robert P. ....Minneapolis
Jo, Wenancio T. ....Minneapolis
Johanson, James E. ....Minneapolis
Johnson, Alan R. ....Minneapolis
Johnson, Angelo G. ....Minneapolis
‡ Johnson, Arthur B. ....Minneapolis
Johnson, Bradley D. ....Minneapolis
Johnson, Curtis A. ....Minneapolis
Johnson, David R. ....Minneapolis
Johnson. Donald A. ....Minneapolis
‡ Johnson, Edward A. ....Minneapolis
‡ Johnson, Frank E. ....Minneapolis
£ Johnson, Frederick W. ....Minneapolis
‡ Johnson, Gordon E. ....Minneapolis
‡ Johnson, Harry A., Jr. ....Minneapolis
†‡ Johnson, James A. ....Minneapolis
‡ Johnson, John W. ....Minneapolis
Johnson, Mark H. ....Minneapolis
† Johnson, Norman P. ....Minneapolis
Johnson, Norman Paul ....Minneapolis
†‡ Johnson, Norton T. ....Minneapolis
‡ Johnson, Paul E. ....Wayzata
‡ Johnson, Phillip S. ....Anoka
‡ Johnson, Reinald G. ....Minneapolis
‡ Johnson, Richard S. ....Minneapolis
‡ Johnson, Richard V. ....Minneapolis
‡ Johnson, Robert E. ....Minneapolis
‡ Johnson, Thomas H., Jr. ....Minneapolis
Johnson, Youbert T. ....Minneapolis
‡ Johnston, Donald K. ....Minneapolis
Jones, David G. ....Minneapolis
†‡ Jones, Herbert W., Jr. ....Minneapolis
‡ Jones, Richard H. ....Minneapolis
‡ Jones, Thomas K., Jr. ....Minneapolis
Jordan, James J. ....Minneapolis
‡ Jorgensen, Harlan ....Minneapolis
Judd, Allen S. ....Minneapolis
† Judd, Walter H. ....Washington, DC
† Jurdy, Mitchell J. ....Minneapolis
Kadesky, Harold B. ....Minneapolis
Kaiser, Harold B. ....Minneapolis
Kalb, Thomas J. ....Minneapolis
†‡ Kallestad, Leonard L. ......Lauderdale-by-the-Sea, FL
Kane, Dennis J. ....Minneapolis
Kane, Morton C. ....Minneapolis
Kane, William J. ....Chicago, IL
‡ Kaplan, Arnold P. ....Minneapolis
*‡ Kaplan, J. Jacob ....Minneapolis
‡ Kaplan, Martin B. ....Minneapolis
‡ Karleen, Conrad I. ....Minneapolis
‡ Karlen, Markle ....Minneapolis
‡ Kasper, Robert E. ....Minneapolis
‡ Katkov, Harold ....Minneapolis
Katz, Beni ....Minneapolis
Katz, Harry I. ....Minneapolis
Kaye, Dale R. ....Minneapolis
Kegel, James F. ....Minneapolis
†‡ Kelby, Gjert M. ....Minneapolis
‡ Keldahl, Loren R. ....Minneapolis
Kelly, Charles F. ....Minneapolis
‡ Kelly, John C. ....Minneapolis
‡ Kelly, John P. ....Minneapolis
‡ Kelly, John T. ....Robbinsdale
Kelly, William D. ....Minneapolis
£ Kemp, Fred V. ....Hopkins
Kennedy, B. J. ....Minneapolis
*† Kennedy, Claude C. ....Minneapolis
‡ Khorsand, Darius ....Minneapolis
Kieffer, Stephen A. ....Minneapolis
Kim, Mark K. ....St. Paul
Kim, Suck Won ....Minneapolis
Kimmel, George C. ....Minneapolis
Kind, Allan C. ....St. Louis Park
† King, Frances W. ....Minnetonka
‡ Kinney, William N. ....Anoka
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‡ Kiser, Joseph C. ....Minneapolis
Kjellsen, Douglas L. ....Minneapolis
Klassen, Arthur C. ....Minneapolis
‡ Kleven, Lowell H. ....Minneapolis
‡ Knapp, Miland E. ....Minneapolis
*† Knight, Ray R. ....Minneapolis
‡ Knobloch, William H. ....Minneapolis
Knowles, Richard A. ....Coon Rapids
Knudsen, Helen L. ....Minneapolis
§ Kolar, Stephen J. ....Minneapolis
Kolars, Charles P. ....Minneapolis
† Koller, Hermann M. ....Minneapolis
Koller, Robert L. ....Minneapolis
Koontz, Peter S. ....Minneapolis
‡ Koos, Gerald W. ....Minneapolis
Korchik, John P. ....Minneapolis
Koropchak, Nicholai ....Minneapolis
‡ Kostich, Nikola D. ....Minneapolis
Kottke, Frederic J. ....Minneapolis
† Koucky, Rudolph W. ....Sagle, ID
‡ Kovack, Freeman D. ....Minneapolis
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‡ Krafft, Walter E. ....Minneapolis
‡ Kragh, Lyle V. ....Minneapolis
Kramer, Daniel W. ....Minneapolis
‡ Kremen, Arnold J. ....Minneapolis

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	Kronenberg, Richard S.	Minneapolis
	Krystosek, Lee A.	Minneapolis
†	Kucera, Frank J.	Hopkins
†	Kucera, William J.	Santa Barbara, CA
‡	Kump, Warren L.	Minneapolis
£	Kuslich, Stephen D.	Burnsville
	Kusz, Clarence V.	Minneapolis
‡	Kyllo, John E.	Minneapolis
‡	Kyllonen, Ronald R.	Edina
	L'Heureux, Philippe R.	Minneapolis
‡	LaBree, John W.	Minneapolis
‡	Lagaard, Sheldon M.	Minneapolis
‡	Lai, Charles C. Y.	Minneapolis
†	Lajoie, John M.	Minneapolis
	Lamb, H. Douglas	Chattahooche, FL
‡	Landsman, Gordon S.	Minneapolis
	Lane, Jerald P.	Minneapolis
	Lang, Leonard A.	Minneapolis
	Langer, Leonard O., Jr.	Minneapolis
‡	Lannon, James B.	Minneapolis
†‡	Lapierre, Arthur P.	Minneapolis
‡	Larsen, Frank W.	Minneapolis
	Larsen, Russel H.	Minneapolis
‡	Larson, Allen K.	Minneapolis
	Larson, Arthur K.	Minneapolis
‡	Larson, Donald M.	Minneapolis
‡	Larson, Ernest J., Jr.	Minneapolis
	Larson, F. Wilmer	Minneapolis
§	Larson, Keith D.	Minneapolis
†‡	Larson, Lawrence M.	Minneapolis
	Larson, Loren J.	Minneapolis
	Larson, Paul H.	Minneapolis
‡	Larson, Richard E.	Minneapolis
‡	Larson, Roger C.	Minneapolis
	Larson, Stephen L.	Edina
	Larson, Wyllis G.	Minneapolis
	Latts, Elliot M.	Minneapolis
	Lauritzen, Herbert	Minneapolis
†	LaVake, Rae T.	Minneapolis
‡	Lavender, Dick R.	St. Louis Park
	Lawrence, Van S.	Minneapolis
	Lawrow, John W.	Minneapolis
	Lawson, Warren R.	Minneapolis
‡	Lawton, James J., Jr.	Minneapolis
‡	Laxdal, Stefan D.	Minneapolis
‡	Layer, James M.	Minneapolis
	Layman, Thomas E.	Minneapolis
	Leavenworth, Richard O., Jr.	Minneapolis
	Lee, Ju Hao	Minneapolis
	Lee, Myoung Chong	Minneapolis
‡	Leemhuis, Andrew J.	Minneapolis
‡	Lees, David C.	Minneapolis
‡	Leiferman, Robert J.	Minneapolis
	Leighton, John S.	Minneapolis
	Leinonen, Wendla E.	Anoka
	Lenz, Bernard W.	Minneapolis
‡	Lenz, Oa	Minneapolis
‡	Leonard, Samuel	Minneapolis
	Lerner, A. Ross	Minneapolis
‡	Leslie, Loren R.	Minneapolis
	Leslie, W. Robert	Minneapolis
	Lester, Theodore H.	Minneapolis
	Letson, Robert D.	Minneapolis
‡	Levine, Howard M.	Minneapolis
	Levine, Norman D.	Minneapolis
‡	Levitt, Seymour H.	Minneapolis
	Levy, Michael	Minneapolis
	Lewis, Glenn M., Jr.	Minneapolis
‡	Lick, Louis C.	Minneapolis
	Liebhaber, Henia F.	Minneapolis
	Lillehei, James P.	Minneapolis
	Lillehei, Richard C.	Minneapolis
‡	Limbeck, Donald A.	Minneapolis
	Lindall, Arnold W., Jr.	Minneapolis
‡	Lindberg, Evan F.	Minneapolis
‡	Lindberg, Vernon L.	Minneapolis
‡	Lindberg, Winston R.	Minneapolis
‡	Lindeland, Arthur T.	Minneapolis
‡	Lindemann, Charles E.	Minneapolis
‡	Linderholm, Bruce E.	Minneapolis
‡	Lindgren, Russell C.	Minneapolis
	Lindquist, Janet M.	Nigeria, W. Africa
	Lindstrom, Richard L.	Minneapolis
‡	Linner, John H.	Minneapolis
‡	Linner, Paul W.	Minneapolis
	Lipschultz, Martin	St. Louis Park
	Lipschultz, Oscar	St. Louis Park
†	Litman, Abraham B.	Minneapolis
‡	Litman, Thomas	Minneapolis
	Lo, Josephine	Minneapolis
	Lober, Paul H.	Minneapolis
‡	Locke, Murray S.	Minneapolis
§	Loes, Michael W.	Minneapolis
§	Loes, Peter L.	Minneapolis
	Lofsness, Stanley V.	Minneapolis
	Loken, Merle K.	Minneapolis
	London, Nathaniel J.	Minneapolis
	Lonstein, John E.	Minneapolis
£	Looney, Timothy J.	Minneapolis
‡	Lott, Frederick H.	Minneapolis
†	Lovett, Beatrice R.	Minnetonka
	Lowe, Douglas A.	Minneapolis
	Lowry, Jeanette K.	Minneapolis
	Lowry, Paul T.	Minneapolis
	Lucas, David D.	Minneapolis
‡	Luckey, William T.	Minneapolis
‡	Lueck, Wallace W.	Minneapolis
*†‡	Lufkin, Nathaniel H.	Minneapolis
	Lukinac, Charles J.	Minneapolis
	Lund, George W.	Minneapolis
	Lund, Nancy R.	Minneapolis
‡	Lund, Richard R.	Minneapolis
‡	Lundblad, Rodger R.	Minneapolis
	Lundblad, Stanley W.	Minneapolis
§	Lunde, Paula A.	Minneapolis
†	Lundeberg, Karl R.	Minneapolis
	Lundquist, Charles B.	Minneapolis
‡	Lundquist, Virgil J. P.	Minneapolis
‡	Lynch, Michael F.	Minneapolis
	Lyon, Fred A.	Minneapolis
	Lyon, John D.	Hopkins
	Lysne, Richard B.	Minneapolis
	Lysyj, Anatol	Minneapolis
	Lyzenga, Anton G.	Minneapolis
	McCaffrey, F. John	Minneapolis
‡	McCannel, Malcolm A.	Minneapolis
†	McCarthy, Donald	Minneapolis
‡	McCollister, Robert J.	Minneapolis
	McConnell, John W.	Wayzata
‡	McCormick, Donald P.	Minneapolis
†	McDaniel, Orianna	Minneapolis
†	McEwan, Alexander	Minneapolis
†	McFarland, Arthur H.	Minneapolis
†	McGandy, Robert F.	Minneapolis
	McGovern, Lawrence	Minneapolis

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Hennepin County Medical Society *(Continued)*

†‡	McInerny, Maurice W.	Minneapolis
†	McKelvey, John L.	St. Paul
	McKelvey, John M.	Minneapolis
	McKenna, James L.	Minneapolis
‡	McKenzie, Charles H.	Minneapolis
	McKhann, Charles F.	Minneapolis
	McKinlay, Gordon L.	Minneapolis
‡	McKinley, C. Richard	Minneapolis
†	McKinney, Frank S.	Minneapolis
	McLaughlin, Byron H.	Minneapolis
	McMahon, John E.	Minneapolis
	McNeil, John J.	Minneapolis
‡	McParland, Felix A., Jr.	Minneapolis
	McQuoid, David W.	Minneapolis
	MacCormick, Robert, Jr.	Minneapolis
†‡	MacDonald, Daniel A.	Minneapolis
‡	MacGibbon, James D.	Minneapolis
‡	MacKinnon, Donald C.	Minneapolis
†‡	Mach, Frank B.	Minneapolis
	Mach, John R.	Minneapolis
	Macheledt, Neil L.	Anoka
	Madireddi, Siuoranak	Osseo
‡	Madsen, Donald O.	Minneapolis
‡	Maeder, Edward C.	Minneapolis
‡	Maeder, Edward C., Jr.	Minneapolis
‡	Magee, Timothy M.	Minneapolis
	Magnuson, Michael C.	Minneapolis
	Mahmud, Kholid	Minneapolis
‡	Malmquist, Carl P.	Minneapolis
	Mandel, Sheldon L.	Minneapolis
	Manick, Kenneth P.	Minneapolis
‡	Mankey, James C.	Minneapolis
	Mann, George A.	Minneapolis
‡	Manoles, Ellias N.	Minneapolis
	Manolis, Deane C.	Minneapolis
‡	Mark, Aaron L.	Minneapolis
‡	Mark, Merle S.	Minneapolis
	Mark, Peter M.	Minneapolis
‡	Marking, George H.	Minneapolis
	Markland. Colin	Minneapolis
	Markovitz, Jack M.	Minneapolis
‡	Marte, Egon	Minneapolis
‡	Martin, Frank E.	Minneapolis
‡	Martin, George R.	Minneapolis
	Martinson, Elmer J.	Wayzata
§	Masem, Mathias A.	Minneapolis
	Maslansky, Robert A.	Minneapolis
‡	Massee, Joseph S.	Minneapolis
	Mastbaum, Leonard I.	Minneapolis
	Mathog, Robert G.	Minneapolis
	Matthews, John A. G.	Minneapolis
	Maunder, John B.	Minneapolis
†	Maxeiner, Stanley R.	Minneapolis
‡	Maxeiner, S. R., Jr.	Minneapolis
	Maxwell, Robert E.	Minneapolis
	Mayberg, Donald M.	Minneapolis
	Meany, Thomas J.	Minneapolis
	Mears, Thomas V.	Minneapolis
‡	Medina. Ambrosio M., Jr.	Wayzata
‡	Meeker, Henry C.	Minneapolis
	Meekin, Patrick C.	Minneapolis
	Meland, Mary H.	Minneapolis
‡	Melichar, Paul J.	Minneapolis
	Meller, Robert L.	Minneapolis
	Mensheha, Nicholas M.	Minneapolis
‡	Merner Thomas B.	Minneapolis
†	Merrick, Charlotte T.	St. Paul
‡	Metz, Donald D.	Minneapolis
	Meyer, Alvin J.	Minneapolis
	Meyer, James J.	Minneapolis
†	Michel, Henry H.	Minneapolis
†	Mickelson, Emma F (Fronk)	Holmes Beach, FL
	Middlebrook, John E.	Minneapolis
‡	Miller, H. Dawes	Minneapolis
‡	Miller, Harold E.	Minneapolis
*†‡	Miller, Hugo E.	Minneapolis
	Miller, J. Carleton	Minneapolis
£	Miller, Kenneth	Apple Valley
	Miller, William P.	Minneapolis
‡	Millett, D. Keith	Minneapolis
	Milroy, Thomas W.	Aberdeen, SD
	Minder, John G.	Minneapolis
	Mindrum, Gerald G.	Minneapolis
	Minsky, Armen A.	Minneapolis
	Mintalar, Jose M.	Minneapolis
‡	Mitby, Irvin L.	Minneapolis
‡	Mitchell, Berton D.	Minneapolis
	Mitchell, Edward C.	College Place, WA
‡	Mitchell, Mancel T.	Minneapolis
‡	Mixer, Harry W.	Minneapolis
	Moe, John H.	Minneapolis
‡	Moe, W. Wyatt	Minneapolis
‡	Moehn, John T.	Minneapolis
†	Moen, Johannes K.	Minneapolis
	Moghaddam, Alaeddin	Minneapolis
‡	Monson, Einer M.	Minneapolis
‡	Monson, Paul S.	Minneapolis
	Monson, Warren A.	Minneapolis
‡	Moody, David L.	Minneapolis
†	Moore, Irvin H.	Eden Prairie
£	Moore, Richard H.	Minneapolis
	Moorhead, Marie	Minneapolis
	Moos, Daniel J.	Minneapolis
£	Moquist, Dale C.	New Hope
‡	Moral, Harvey M.	Minneapolis
	Morgan, John C.	Minneapolis
	Moriarty, James A.	Minneapolis
	Moriarty, Joseph D.	Minneapolis
‡	Mork, A. Harold	Anoka
‡	Mork, Frank E.	Anoka
‡	Mork, Frank E., Jr.	Minneapolis
	Moss, Nyel H.	Minneapolis
‡	Mosser, Donn G.	Minneapolis
	Mossman, Philip L.	Minneapolis
‡	Moyer, Leonard B.	Minneapolis
	Mueller, Henry M.	Minneapolis
‡	Mueller, James M.	Minneapolis
‡	Mulholland, William M.	Minneapolis
‡	Mullin, Gerald T., Jr.	Minneapolis
‡	Mulvahill, John E.	Minneapolis
‡	Munkittrick, Ronald C.	Minneapolis
	Murdock, David K.	Minneapolis
	Murray, Charles L.	Minneapolis
†	Murray, Elisabeth M.	Minneapolis
	Muschenheim, Frederick	Minneapolis
‡	Muske, Marvin M.	Minneapolis
#	Musty, Michael O.	Minneapolis
	Musty, Nicholas J.	Minneapolis
†	Myers, Jay A.	Minneapolis
‡	Myhre, James	Minneapolis
	Mylrea, Murray J.	Burnsville
	Nagobads, Ilgvars J.	Minneapolis
	Nagobads, V. George	Minneapolis
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	Nash, Eldore B.	Minneapolis
	Nathenson, Aaron L.	Minneapolis
†‡	Neal, Joe M.	Minneapolis

Hennepin County Medical Society *(Continued)*

	Neal, Robert R., Jr.	Minneapolis
†	Nelson, Bernice A.	Minneapolis
†	Nelson, C. Barton	Minneapolis
	Nelson, Carleton A.	Minneapolis
£	Nelson, David W.	Minneapolis
‡	Nelson, Edward N.	Minneapolis
	Nelson, Evan L. Jr.	Minneapolis
‡	Nelson, Glen D.	Minneapolis
‡	Nelson, Gunard A.	Minneapolis
†	Nelson, Harvey	Deerfield Beach, FL
‡	Nelson, Lloyd S.	Minneapolis
	Nelson, Maxine O.	Minneapolis
‡	Nelson, Maynard C.	Minneapolis
‡	Nelson, O. L. Norman	Minneapolis
†‡	Nelson, Wallace I.	Minneapolis
	Nemanich, George J.	Minneapolis
	Nerenberg, Sidney	Minneapolis
	Nesse, Anton S.	Minneapolis
‡	Nesset, Lawren B.	Minneapolis
‡	Nesset, William D.	Minneapolis
	Neumann, Roland F.	Minneapolis
‡	Neumeister, Charles A.	Minneapolis
	Neuwirth, Gerardo D.	Golden Valley
	Nicholas, S. Scott, Jr.	Minneapolis
	Nicolette, Charles C.	Minneapolis
	Nielsen, David J.	Minneapolis
‡	Nilsen, John A.	Minneapolis
	Nivatvonges, Sathat	Minneapolis
	Nolan, Robert K.	Brooklyn Center
‡	Noran, Harold H.	Minneapolis
£‡	Nordberg, William J.	St. Louis Park
‡	Nord, Robert E.	Minneapolis
£	Nordlie, Paul E.	Minneapolis
‡	Norman, Franklin C.	Minneapolis
‡	Norman, Mark L., Jr.	Minneapolis
	Norval, Mildred A.	Minneapolis
‡	Nuessle, William F.	Minneapolis
	Nussbaum, Daniel	Minneapolis
‡	Nydahl, Bruce C.	Minneapolis
†‡	Nydahl, Malvin J.	Minneapolis
‡	O'Brien, Bruce J.	Minneapolis
£	O'Brien, Daniel K.	Minneapolis
‡	O'Brien, William A.	Minneapolis
†	O'Donnell, James E.	Minneapolis
	O'Hanlon, William J.	Minneapolis
‡	O'Leary, John B.	Minneapolis
	O'Neil, Bernerd L.	Minneapolis
‡	O'Phelan, E. Harvey	Minneapolis
	Officer, Charles D.	Burnsville
§	Ogle, Richard G.	Lakeville
	Ohmann, Ronald J.	Minneapolis
	Okagaki, Takasho	Minneapolis
	Olavs, Olga	Minneapolis
‡	Olfelt, Paul C.	Minneapolis
†	Olsen, E. George	Minnetonka
	Olsen, Jay R.	Minneapolis
	Olson, Alton C.	Minneapolis
	Olson, C. Kent	Minneapolis
	Olson, Carl J.	Minneapolis
	Olson, Daniel J.	Minneapolis
‡	Olson, Detlof M.	Minneapolis
‡	Olson, Duane C.	Minneapolis
‡	Olson, Hardin E.	Minneapolis
‡	Olson, Philip A.	Minneapolis
	Olson, Philip K.	Minneapolis
	Olson, Richard A.	Minneapolis
‡	Olson, Robert A.	Minneapolis
	Olson, Robert E.	Minneapolis
	Olson, Robert W.	Minneapolis
	Olson, Rolland A.	Wayzata
‡	Opheim, Richard H.	Minneapolis
‡	Oppen, E. Gerhard	Minneapolis
	Oppen, Melvin G.	Minnetonka
	Opstad, Earl T.	Minneapolis
	Orbuch, Martin W.	Minneapolis
	Orkin, Milton	Minneapolis
	Orn, Duane L.	Minneapolis
	Osterberg, Kenneth A.	Minneapolis
	Ostrov, Charles S.	Minneapolis
	Ott, Eugene C.	Minneapolis
	Owen, Richard R.	Minneapolis
	Paal, Dwain J.	Minneapolis
†	Page, Raymond L.	St. Paul
‡	Paisner, Hyman M.	Minneapolis
†	Palen, Benjamin J.	Scottsdale, AZ
‡	Paparella, Michael M.	Minneapolis
	Papermaster, Ralph	Minneapolis
	Papermaster, Theodore C.	St. Louis Park
†	Park, Wilford E.	Minneapolis
	Parod, John D.	Minneapolis
‡	Parrott, John C.	Minneapolis
	Pass, Franklin	Minneapolis
	Pattee, James J.	Minneapolis
‡	Patterson, Paul G.	Minneapolis
£	Payne, Eliz E.	Minnetonka
	Paule, William J.	Minneapolis
‡	Peluso, Charles R.	Minneapolis
	Pennington, Mary	Minneapolis
‡	Peper, Martin C.	Minneapolis
‡	Perlman, Everett C.	Minneapolis
	Perlman, Herschel L.	St. Louis Park
‡	Peteler, Jennings C. L.	Minneapolis
	Peters, John R.	St. Louis Park
	Petersen, Byron D.	Minneapolis
‡	Petersen, Deane A.	Minneapolis
‡	Petersen, Glenn L.	Minneapolis
	Petersen, William E.	Minneapolis
	Peterson, Charles A.	Minneapolis
	Peterson, Charles R.	Minneapolis
	Peterson, John A.	Minneapolis
‡	Peterson, Oliver H.	Minneapolis
	Peterson, Palmer A.	Minneapolis
‡	Peterson, Rodney H.	Minneapolis
‡	Peterson, Theodore A.	Minneapolis
‡	Peterson, Willard C.	Minneapolis
‡	Petit, Julien V.	Minneapolis
*†	Petit, Leon J.	Minneapolis
‡	Pewters, John T.	Minneapolis
‡	Pfohl, Richard A.	Minneapolis
†	Phelps, Kenneth A.	Palo Alto, CA
	Phelps, Robert D.	Minneapolis
	Phibbs, Clifford M., Jr.	Minneapolis
‡	Pilling, Loran F.	Minneapolis
	Pincus, Mitchell	Minneapolis
	Pizarro, Remi L.	Minneapolis
‡	Plasha, Matt K.	Coon Rapids
	Plass, Herbert F. R.	Minneapolis
	Pleissner, Karl W.	Minneapolis
	Plimpton, Nathan C.	Minneapolis
	Pohl, John F.	Minneapolis
£	Poland, Jerome D.	Minneapolis
	Polesky, Herbert F.	Minneapolis
	Poley, Brooks J.	Minneapolis
	Poljack, Stuart J.	Minneapolis
	Pollak, Kurt	Minneapolis
‡	Pollock, Anthony J.	Minneapolis
*†‡	Polzak, James A.	Roseville

(Continued on next page)

Hennepin County Medical Society *(Continued)*

†	Pone, John J.	Minneapolis
‡	Popadiuk, Peter	Minneapolis
‡	Popowich, John G.	Minneapolis
	Potter, Robert B.	Minneapolis
†	Pratt, Fred J.	Minneapolis
	Prawer, Steven	Minneapolis
‡	Prem, Konald A.	Minneapolis
	Preston, Frank S.	Minneapolis
‡	Price, William E.	Minneapolis
‡	Prickman, William E.	Minneapolis
‡	Priest, Robert E.	Minneapolis
	Probstfield, Jeffrey L.	Minneapolis
	Proshek, Lumir C.	Minneapolis
£	Pyle, Robert B.	Minneapolis
‡	Quello, Robert O. B.	Minneapolis
‡	Quick, Cedric A.	Minneapolis
	Quiggle, Arthur B.	Minneapolis
‡	Quist, Henry W., Jr.	Minneapolis
	Raab, David E.	Minneapolis
	Racer, Harley J.	Minneapolis
	Ragan, John J.	Minneapolis
	Raich, John J.	Minneapolis
‡	Raile, Richard B.	Minneapolis
£	Ramos, Marcos	Minneapolis
	Randall, David A.	Minneapolis
‡	Randall, Philip S.	Minneapolis
	Ranheim, Phillip J.	Minneapolis
‡	Ratelle, Alexander E.	Minneapolis
	Ray, Charles D.	Minneapolis
	Recht, Thomas M.	Minneapolis
£	Reder, Michael S.	Roseville
	Reece, Richard L.	Minneapolis
‡	Reed, John H., Jr.	Minneapolis
	Reed, Sheldon C.	Minneapolis
‡	Regan, John J.	Minneapolis
	Rehmann, Ronald E.	Coon Rapids
	Reichel, Samuel M.	Minneapolis
	Reichert, John A.	Minneapolis
‡	Reif, Harold A.	Minneapolis
‡	Reiley, Richard E.	Minneapolis
	Reinhardt, James H.	Minneapolis
‡	Reinhart, Richard O.	Minneapolis
	Reisdorf, George E.	St. Louis Park
‡	Reiser, Milton P.	Minneapolis
‡	Remple, William D.	Minneapolis
	Resch, Joseph A.	Minneapolis
	Reul, Thomas W.	Robbinsdale
	Reynolds, James	Minneapolis
	Rholl, Arnold O.	Minneapolis
†‡	Rice, Carl O.	Minneapolis
	Rice, Edwin G.	Minneapolis
	Rice, Fred A.	Minneapolis
‡	Richardson, Robert J.	Minneapolis
‡†	Richdorf, Lawrence F.	Minneapolis
	Richmond, Harvey S.	Minneapolis
‡	Rierson, Phillip A.	Minneapolis
	Riley, John D.	Minneapolis
	Riordan, Elsie M.	Minneapolis
	Ripple, Rudolph J., Jr.	Minneapolis
‡	Risch, Ronald E.	Minneapolis
	Rizer, Dean K.	Minneapolis
†	Robb, Edwin F.	Boca Raton, FL
	Roberts, Byron H.	Minneapolis
‡	Roberts, Lewis J.	Minneapolis
	Robinson, Cortland O.	Minneapolis
	Rock, William H.	Anoka
‡	Rocknem, Robert E.	Minneapolis
	Rockwell, Curtiss V.	Minneapolis
‡	Rodgers, Richard S.	Minneapolis
	Rodman, William W.	Coon Rapids
	Rogin, Norton	Minneapolis
	Rohrmann, Charles A., Jr.	Minneapolis
	Rollins, Pat	Minnetonka
	Romness, Kenneth B.	Mound
	Rosenbaum, David L.	Minneapolis
‡	Rosendahl, Frederick G.	Minneapolis
	Rosenberg, Laurence J.	Wayzata
	Rosenberg, Robert H.	Minneapolis
	Rotenberg, Samuel	Huntington Park, CA
†	Rosenfield, Abraham B.	Minneapolis
	Rosenow, John H.	Minneapolis
‡	Rosenquist, Rudolph J.	Minneapolis
	Rosenstein, Hanan J.	Minneapolis
*‡	Rosenwald, Reuben M.	Anoka
‡	Rossen, Ralph	Minneapolis
	Rotenberg, Robert J.	Minneapolis
‡	Rothnem, Morris S.	Minneapolis
	Rotta, James R.	Minneapolis
	Rubin, Manly	Minneapolis
	Rucker, Thomas K.	Minneapolis
†	Rucker, William H.	Minneapolis
†	Rud, Norman E.	Edina
‡	Ruiz, Ernest	Minneapolis
‡	Russeth, Arthur N.	Minneapolis
†‡	Rusten, Elmer M.	Minneapolis
	Rydberg, John S.	Minneapolis
	Rydland, Arne D.	Minneapolis
	St. Cyr, Harry M.	Minneapolis
§	St. Cyr, John A.	Minneapolis
†	St. Cyr, Kenneth J.	Minneapolis
	Salchert, John J.	Minneapolis
†‡	Saliterman, Bernard I.	Minneapolis
‡	Salovich, Edward L.	Minneapolis
‡	Salovich, Elmer R.	Minneapolis
	Sanchez, Jose S.	W. St. Paul
‡	Sandt, Karl E.	Minneapolis
	Sane, Kumud S.	Minneapolis
	Sane, Shashikant M.	Minneapolis
	Sanfilippo, Sylvester J.	Minneapolis
	Sartor, Richard	Minneapolis
	Sauer, Jean C.	Minneapolis
	Sawyer, Glen T.	Minneapolis
	Sayther, Keith D.	Minneapolis
‡	Sborov, Abe M.	Minneapolis
	Scallen, Raymond W.	Minneapolis
‡	Scanlan, Patrick J.	Minneapolis
	Schaar, Frances E.	Minneapolis
†	Schaefer, Wesley G.	Edina
	Schaffhausen, Irwin F.	Minneapolis
	Schaffhausen, Mildred	Minneapolis
‡	Scherer, L. Raymond	Minneapolis
	Scherling, Sidney S.	Minneapolis
‡	Schiele, Burtrum C.	Minneapolis
£‡	Schiller, Philip J.	Minneapolis
#	Schissel, Gregory A.	New York, NY
‡	Schissel, Richard C.	Minneapolis
‡	Schmidt, W. Robert	Minneapolis
†	Schmitt, Samuel C.	Fallbrook, CA
	Schneck, Jack I.	Minneapolis
	Schoening, Herbert A.	Minneapolis
‡	Schoenwetter, William F.	Minneapolis
‡	Schottler, Jerry L.	Minneapolis
*†	Schottler, Max E.	Minneapolis
‡	Schroeder, Albert J.	Minneapolis
	Schultz, Alan	Minneapolis
	Schultz, Alvin L.	Minneapolis
‡	Schultz, J. Harold	Minneapolis

Hennepin County Medical Society *(Continued)*

‡	Schultz, Peter J.	Minneapolis
	Schultz, Robert J.	Minneapolis
‡	Schulze, William M.	Minneapolis
‡	Schumacher, John W.	Minneapolis
£	Schumacher, Robert V.	Minneapolis
‡	Schut, Lawrence J.	Minneapolis
	Schwartz, E. Robert	Minneapolis
	Sciarra, John J.	Minneapolis
§	Scott, David	Minneapolis
‡	Scott, Horace G.	Minneapolis
£	Scott, John C.	Bloomington
‡	Scott, Robert H.	Minneapolis
	Scott, William R.	Minneapolis
†	Seaberg, John A.	Pequot Lakes
	Seay, James E., III	Minneapolis
	Segal, Edward L.	Minneapolis
	Segal, Martin A.	Minneapolis
	Segal, Marvin S.	Minneapolis
‡	Segal, Sheldon J.	Minneapolis
†	Seham, Max	St. Paul
	Seifert, Gregory L.	Minneapolis
	Seifert, Milton H., Jr.	Excelsior
‡	Seljeskog, Edward L.	Minneapolis
	Semba, Thomas	Minneapolis
‡	Semsch, Robert D.	Wayzata
	Severseike, Odean M.	Minneapolis
§	Severson, Michael V.	Minneapolis
‡	Seymour, John L.	Minneapolis
	Shackelford, Terry C.	Minneapolis
‡	Shah, Popatial S.	Osseo
	Shah, Ranjana N.	Minneapolis
‡	Shandorf, James F.	Minneapolis
	Shanks, James R.	Minneapolis
†	Shaperman, Eva P.	San Diego, CA
	Shapiro, Irving	Minneapolis
	Shapiro, Sidney K.	Minneapolis
‡	Shapiro, Stanley W.	Minneapolis
‡	Shattuck, Clark A.	Minneapolis
‡	Shaw, Howard A.	Minneapolis
	Shea, Andrew W.	Minneapolis
‡	Shemesh, Alvin	Minneapolis
	Sher, Lewis	Minneapolis
‡	Sherman, Lloyd F.	Minneapolis
†	Shillington, Maurice A.	Ft. Lauderdale, FL
	Sholler, Lawrence J.	Minneapolis
£	Shons, Alan R.	Edina
	Shragg, Robert I.	Minneapolis
	Shronts, John F.	Minneapolis
	Shronts, John S.	Minneapolis
	Sidell, Franklin D.	Minneapolis
	Siebert, Richard C.	Minneapolis
	Siegmann, William C.	Minneapolis
‡	Sigel, Melvin E.	Minneapolis
	Sigelman, Robert J.	Minneapolis
‡	Silas, Ralph M.	Minneapolis
	Silver, John D.	Minneapolis
‡	Silverstein, Paul M.	Minneapolis
‡	Simmons, Richard K.	Minneapolis
	Simmons, Richard L.	Minneapolis
	Simo, Kathleen Kay	Minneapolis
‡	Simonson, Donald B.	Minneapolis
§	Simonson, Richard B.	Minneapolis
‡	Simso, Lee A.	Minneapolis
	Singher, Lawrence J.	Minneapolis
‡	Sinykin, Melvin B.	Minneapolis
	Sipe, James W.	Coon Rapids
	Siruno, Eugenio S.	Minneapolis
	Skjold, Arthur C.	Minneapolis
‡	Sletten, Richard G.	Minneapolis
‡	Slosser, Gaius, J., II	Minneapolis
	Smeby, Loren A.	Robbinsdale
	Smelker, Jean	Minneapolis
	Smiley, John T.	Minneapolis
†‡	Smisek, Frank M.	Minneapolis
*†	Smith, Adam M.	Minneapolis
‡	Smith, Archie M.	Minneapolis
	Smith, Barlow	Minneapolis
‡	Smith, Graham G.	Minneapolis
	Smith, Henry T.	Minneapolis
§	Smith, James M.	Minneapolis
‡	Smith, John E.	Minneapolis
	Smith, Nadine G.	Minneapolis
‡	Smith, Theodore S.	Minneapolis
‡	Soderberg, Richard J.	Minneapolis
†‡	Soderlind, Ragnar T.	Minneapolis
‡	Soiseth, Robert P.	Minneapolis
§	Solhaug, Michael J.	Minneapolis
‡	Solhaug, Samuel B., Jr.	Minneapolis
	Solvason, Harold M.	Minneapolis
‡	Spano, Joseph P.	Minneapolis
‡	Spencer, Bernard J.	Minneapolis
	Spencer, David L.	Minneapolis
	Spenny, Edward A. L.	Minneapolis
	Sperling, Keith B.	Minneapolis
	Spink, Wesley W.	Minneapolis
‡	Sponsel, Kenath H.	Minneapolis
£	Springrose, James V.	Minneapolis
‡	Stahr, Aubrey C.	Hopkins
†	Stanford, Charles E.	Waupun
	Stansbury, John A.	Minneapolis
‡	Steidl, Richard M.	Minneapolis
†‡	Stelter, Lloyd A.	Minneapolis
†	Stenstrom, Annette T.	Grand Marais
	Stenwick, Michael W.	Minneapolis
	Stenzel, Donald A.	Minneapolis
	Stenzel, Joseph A.	Minneapolis
	Stephens, William E.	Minneapolis
	Sterrie, Norman A.	Minneapolis
	Stevens, Sheridan S. H.	Minneapolis
	Stewart, Marvin J.	Minneapolis
‡	Stiegler, Farrell S.	Minneapolis
‡	Stilman, M. Thomas	Rochester
‡	Stoltz, Robert C.	Minneapolis
‡	Stone, Norman F.	Minneapolis
	Stone, Stanley P.	Minneapolis
	Strait, Herbert S.	Fridley
‡	Strand, Clarence M.	Minneapolis
	Strand, Peter J.	Minneapolis
	Strand, Richard C.	Minneapolis
	Streu, Richard E.	Minneapolis
‡	Strickler, Jacob H.	Minneapolis
§	Stringer, Gene C.	Minneapolis
	Strobel, Jack L.	Minneapolis
	Strom, Gordon W.	Minneapolis
‡	Strom, Robert L.	Minneapolis
‡	Stromgren, Delph T.	Minneapolis
	Stromme, William B.	Minneapolis
*	Strunk, Clarence A.	Minneapolis
‡	Student, Richard E.	Minneapolis
	Sturgeon, Richard R.	Minneapolis
‡	Sturges, Robert L.	Minneapolis
	Subak, Barbara H.	Minneapolis
‡	Subby, Walter	Minneapolis
	Sukov, Marvin	Minneapolis
‡	Sulciner, Aurel	Minnetonka
	Summar, M. Thomas	Minneapolis
‡	Sundberg, A. Bruce	Minneapolis

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Hennepin County Medical Society *(Continued)*

‡	Sutherland, John E.	Minneapolis
	Swaiman, Kenneth F.	Minneapolis
‡	Swallen, Thomas O.	Minneapolis
	Swanson, David A.	Minneapolis
‡	Swanson, Gerald E.	Minneapolis
	Swanson, John O.	Minneapolis
#	Swanson, Wallace L.	Quito, Ecuador
†‡	Sweetser, Horatio B.	Minneapolis
‡	Sweetser, Theodore H., Jr.	Minneapolis
‡	Swendseen, Carl J.	Minneapolis
	Swenson, Floyd J.	Minneapolis
	Swenson, James D.	Minneapolis
	Swenson, Richard W.	Minneapolis
	Swift, Dean C.	Minneapolis
	Symchych, Boris E.	Minneapolis
	Tagatz, George E.	Minneapolis
‡	Tam, Ernest C.	Minneapolis
‡	Tambornino, Joseph M.	Minneapolis
	Tanaka, Shin	Minneapolis
‡	Tangen, George V.	Minneapolis
	Tanghe, Jan H.	Minneapolis
†	Taylor, Joseph H.	Ft. Lauderdale, FL
‡	Tchou, Mien-Fa	Minneapolis
‡	Telander, Robert L.	Minneapolis
	tenBensel, Robert W.	Minneapolis
‡	Tenner, Robert J.	Minneapolis
‡	Teska, Byron A.	Minneapolis
‡	Teynor, Joseph W.	Minneapolis
‡	Tharp, Ralph	Minneapolis
	Thelemann, Arthur R., Jr.	Minneapolis
	Theobalt, Inge M.	Minneapolis
‡	Theologides, Anthanasios	Minneapolis
	Thomasson, Robert D.	Minneapolis
	Thomes, A. Boyd	Minneapolis
	Thompson, Arthur	Minneapolis
	Thorson, Stuart V.	Minneapolis
	Thysell, Desmond M.	Minneapolis
	Tierney, Jon P.	Minneapolis
	Titrud, Leonard A.	Minneapolis
	Tiu, Ofelio D.	Fridley
‡	Tobin, John A.	St. Paul
	Tobin, John D.	Minneapolis
	Tombers, Joseph M.	Minneapolis
‡	Torp, William B.	Minneapolis
	Torres, Fernando	Minneapolis
	Town, Louise A.	Minneapolis
	Townes, C. Dwight, Jr.	Minneapolis
	Trach, Benedict B.	Minneapolis
	Trost, Francis J.	Minneapolis
‡	Trow, James E.	Minneapolis
	Tsai, Shih Hao	Minnetonka
‡	Tucker, Richard C.	Minneapolis
	Tudor, Richard B.	Minneapolis
£	Tully, Timothy E.	Anoka
	Turbak, Charles E.	Minneapolis
	Turkbas, Nejat	Minneapolis
‡	Twidwell, Joseph E.	Minneapolis
#	Ulrich, Wesley D.	Mafraq, Jordan
‡	Ulvestad, Harold S.	Minneapolis
‡	Utendorfer, Robert W.	Minneapolis
‡	Vaaler, Robert T.	Minneapolis
‡	Valgemae, Romil	Minneapolis
	Van Oppen, Dirk J. A.	Minneapolis
	Van Tassel, Robert A.	Minneapolis
	Vellek, Donald G.	Minneapolis
‡	Verby, John E.	Minneapolis
£	Vessey, Ronald R.	Minneapolis
	Vik, A. Elliott	Minneapolis
	Vilaseca, Louis B.	Minneapolis
‡	Villella, Ronald L.	Anoka
	Visscher, Maurice B.	Minneapolis
‡	Von Drashek, Stanley C.	Minneapolis
	von Weiss, David L.	Minneapolis
	Vorlicky, Loren N.	Minneapolis
	Waeschle, Richard K.	Minneapolis
	Wagner, Christian J.	Minneapolis
‡	Wagner, Robert M.	Minneapolis
†	Waldron, Carl W.	Scottsdale, AZ
‡	Waldron, John F.	Minneapolis
	Walker, Fredric E., Jr.	Minneapolis
‡	Walker, James K.	Anoka
	Wall, Carl R.	Grand Marais
	Wallinga, Jack V.	Minneapolis
†	Walonick, Albert L.	Minneapolis
	Walsh, John G.	Minneapolis
	Waltz, Arthur G.	Minneapolis
	Wang, Josef K.	Minneapolis
	Wang, Kyuhyun	Minneapolis
	Wang, Yang	Minneapolis
†	Wangensteen, Owen H.	Minneapolis
‡	Warren, John W.	Minneapolis
	Waterbury, Richard C	Minneapolis
‡	Watson, C. Gordon	Minneapolis
	Watson, Cecil J.	Minneapolis
	Wattenberg, Lee W.	Minneapolis
‡	Weatherhead, D. Stuart P.	Minneapolis
‡	Webber, Richard J.	St. Paul
‡	Weber, Lowell W.	Minneapolis
#	Wegleitner, Mark J.	Washington DC
	Weisberg, Martin G.	Minneapolis
	Weisberg, Rapheal J.	Minneapolis
	Weisberg, Stephen C.	Minneapolis
	Weisel, Mary R.	St. Paul
	Wempner, Robert L.	Chaska
‡	Wendland, John P.	Minneapolis
	Wengler, Robert A.	Minneapolis
	Werges, Thomas M.	Minneapolis
	Werner, George	Minneapolis
‡	Wesolowski, Stanley	St. Paul
†	West, Catherine C.	Edina
	West, William P.	Minneapolis
	Wester, Mary Sue	Minneapolis
‡	Westgate, Hugh D.	Minnetonka
	Westreich, Gilbert	Minneapolis
†	Wetherby, Macnider	Minneapolis
	Wethington, Joseph F.	Coon Rapids
‡	Wett, Richard J.	Minneapolis
	Wexler, Harold M.	Minneapolis
‡	Wheeler, Robert W.	Minneapolis
	Whitacre, John C., II	Minneapolis
	White, Asher A.	Minneapolis
†	White, Willard D.	Edina
†	Whitesell, Lloyd A.	Minneapolis
	Wicklund, Paul E.	Wayzata
	Widdifield, David R.	Minneapolis
‡	Widen, Wilford F.	Minneapolis
	Wiens, Cornelius W.	Minneapolis
‡	Wigdahl, Lowell C.	Fridley
‡	Wigdahl, Luther O.	Minneapolis
	Wigg, Norman P.	Minneapolis
‡	Wilcox, William A.	Minneapolis
	Wild, John J.	Minneapolis
†	Wilder, Russell M., Jr.	Topeka, KS
‡	Wilder, Walter L.	Minneapolis
†‡	Wilken, Paul A.	Minneapolis
†	Williams, Henry L.	West St. Paul
‡	Williams, Paul A.	Minneapolis
	Williams, Richard E.	Robbinsdale

Hennepin County Medical Society *(Continued)*
Wilson, John A. ....Minneapolis
‡ Wilson, Robert E. ....Minneapolis
‡ Wilson, Thomas M., Jr. ....Minneapolis
Winchell, Paul ....Minneapolis
Winge, Herbert ....Minneapolis
Winter, Laurence E. ....Minneapolis
† Winther, Nora M. C. ....Columbus, OH
‡ Wippermann, Frederic F. ....Minneapolis
‡ Wisiol, Erich S. ....Minneapolis
Wisness, Osmund A. ....Savage
Woellner, Richard C. ....Minneapolis
‡ Wohlrabe, A. Cabot ....Minneapolis
†‡ Wohlrabe, Arthur A. ....Minneapolis
‡ Wohlrabe, Robert G. ....Minneapolis
Wolter, Frederick H. ....Minneapolis
Wong, Edward T. ....Minneapolis
Wong, Freeman E. ....Minneapolis
£ Wong, Howard H. ....Bloomington
£ Won Savage, Robert L. ....Minneapolis
Woodbury, John W. ....Minneapolis
Woodley, Donald W. ....Edina
‡ Worrell, Philip J. ....Minneapolis
§ Wosing, Robert A., Jr. ....Minneapolis
‡ Woyda, William C. ....Minneapolis
Wright, Donald L. ....Minneapolis
Wright, Francis S. ....Minneapolis
Wright, William S. ....Minneapolis
Wuest, Frederick C. ....Wayzata
† Wynne, Herbert M. N. ....Wayland, MA
Yeager, Terrell F. ....Anoka
Yelle, Matthew D. ....Anoka
†‡ Ylvisaker, Ragnvald S. ....Minneapolis
Yonehiro, Earl G. ....Minneapolis
‡ Young, Ronald C. ....St. Paul
Yue, Wen Y. ....Excelsior
Zahrendt, O. Lewis ....Minneapolis
Zak, Solomon J. ....Minneapolis
£ Zanna, Martin T. ....Minneapolis
Zarling, V. Richard ....Minneapolis
‡ Zaworski, Leo A. ....Minneapolis
Zeise, James A., Jr. ....Minneapolis
‡ Zelickson, Alvin S. ....Minneapolis
† Zierold, Arthur A. ....Minneapolis
Zimering, Sabina ....Minneapolis
‡ Zinn, Charles W. ....Wayzata
‡ Zinter, Ferdinand A. ....Minneapolis

LYON-LINCOLN COUNTY MEDICAL SOCIETY

Lyon and Lincoln Counties
Regular meetings, 6 meetings—Spring and Fall
Annual meeting, November
Number of members 20

PRESIDENT
Hedenstrom, P. C. ....Marshall
SECRETARY
Kaczrowski, William ....Marshall
‡ Eckdale, John E. ....Marshall
‡ Hedenstrom, Philip C. ....Marshall
†‡ Johnson, C. Percy ....Tyler
‡ Kaczrowski, William ....Marshall
Lee, Norman J. ....Tracy
Magtibay, Meynardo B. ....Tyler
‡ Monson, Leonard J. ....Canby
‡ Mueller, LeRoy E. ....Hendricks
‡ Mulder, Richard D. ....Ivanhoe
‡ Murphy, Joseph E. ....Marshall
‡ Myers, John W. ....Canby
‡ Olson, Robert T. ....Canby
‡ Panning, Wayne P. ....Marshall
‡ Peterson, Kenneth A. ....Marshall
† Rohrer, Christian A. ....Madison Lake
‡ Stover, Laddie E. ....Marshall
‡ Taintor, Ronald W. ....Marshall
Tan, Rudy ....Marshall
‡ Thompson, Carl O. ....Hendricks
*† Workman, Warner G. ....Tracy
† Yaeger, Wilbert W. ....Torrance, CA

McLEOD COUNTY MEDICAL SOCIETY

McLeod County
Regular meetings, third Thursday of each month
Annual meeting, November
Number of members 16

PRESIDENT
McNeil, M. R. ....Glencoe
SECRETARY
Kleinkauf, Thomas ....Hutchinson
‡ Bretzke, Carl O. ....Hutchinson
Close, Gerald A. ....Glencoe
Griebie, Grant L. ....Hutchinson
Hegrenes, Robert L. ....Hutchinson
‡ Huebert, Dan W. ....Silver Lake
‡ Jensen, Alvin M. ....Brownton
Ketola, Tauno E. ....Glencoe
‡ Kleinkauf, Thomas P. ....Hutchinson
Leach, T. C. ....Glencoe
McNeil, Maurice R. ....Glencoe
Navratil, Donald R. ....Glencoe
‡ Peterson, Kenneth H. ....Hutchinson
Remucal, H. Chris ....Hutchinson
‡ Smith, George R. ....Hutchinson
‡ Smyth, John J. ....Lester Prairie
Truesdale, Clark W. ....Glencoe

MID-MINNESOTA MEDICAL SOCIETY

Kandiyohi, Meeker, Redwood, Renville and Swift Counties
Regular meetings, third Thursday of each month
Annual meeting in November
Number of members 77

	PRESIDENT	
	Flinn, James	Redwood Falls
	SECRETARY	
	Munneke, Lyle	Clara City
‡	Allison, David D.	Litchfield
	Anderson, Chester A.	Madison
	Bergstrom, John G.	Cokato
	Bosland, Howard G.	Rochester
‡	Brace, Ray I.	Willmar
	Ceplecha, S. Francis	Redwood Falls
	Chunn, Stanley S.	Willmar
	Cosgriff, James A., Jr.	Olivia
	Danielson, Lennox	Litchfield
*	Dille, Donald E.	Litchfield
	Docksey, John W.	Willmar
	Dreyling, Roger A.	Eden Valley
‡	Dunstan, Paul L.	Willmar
	Eberley, Tobe S.	Benson
	Eichelberger, Dale L.	Willmar
‡	Ellinger, Albert J.	Willmar
†	Fawcett, Arthur M.	Renville
	Fedders, Skaidrite C.	Hastings
‡	Fedor, Robert D.	Willmar
‡	Flinn, James B.	Redwood Falls
†	Frederickson, Alice C.	Willmar
‡	Furr, Leo O.	Bird Island
	Gaebe, Milton B.	Clara City
†	Giere, Silas W.	Benson
‡	Gilman, Lloyd C.	Willmar
	Griffin, Richard P.	Benson
‡	Guy, Jack A.	Clara City
‡	Halme, W. B.	Willmar
	Hazen, Richard W.	Willmar
	Hetzler, John A.	Willmar
‡	Hinderaker, Harris P.	Willmar
‡	Hinz, Walter E.	Willmar
	Hodapp, Robert V.	Willmar
	Houts, Joseph C.	Dassel
‡	Iverslie, Phillip C.	Willmar
	Jacobs, Douglas L.	Willmar
	Johnson, Daniel A.	Litchfield
‡	Jorgensen, Donald R.	Willmar
	Kaminski, Gregory W.	Redwood Falls
	Kaufman, Edward J.	Appleton
	Lackore, Leonard K.	Willmar
‡	Larrabee, Walter F.	Willmar
	Leitch, Cecil	Litchfield
	Lenz, Joseph R.	Morton
‡	McAfee, David K.	Willmar
	McCarthy, Austin M.	Willmar
†	Macklin, William E., Jr.	Litchfield
	Maitland, Edwin T.	Willmar
‡	Malone, Patrick M.	Willmar
‡	Mattson, Donald S.	Willmar
	Meinert, John K.	Willmar
‡	Michels, Roger P.	Willmar
	Munneke, Lyle	Clara City
‡	Nelson, Glenn E.	Redwood Falls
	Nelson, Robert H.	Benson
	Nolen, William A.	Litchfield
‡	Olson, Gregory M.	Litchfield
‡	Opsahl, Lawrence J.	Willmar
	Petersen, Donald H.	Willmar
‡	Peterson, Willard E.	Willmar
‡	Proeschel, Ray K.	Willmar
#	Robinson, William W.	Agana, Guam
	Robnik, Spencer L.	Willmar
	Rorem, Joseph A.	Appleton
	Ruchie, Warren H.	Willmar
	Ruhe, Albert H.	Willmar
	Rygh, Harold N.	Atwater
	Sadd, Milton F.	Willmar
‡	Salter, Wilson M.	Willmar
	Schnell, Frederick S.	Litchfield
‡	Schroeppel, Roger	Redwood Falls
	Skaife, William F.	Benson
‡	Strand, Roger W.	Willmar
‡	Strauchler, John	Belview
‡	Tiede, James J.	Wilmot
	Thompson, Russell A.	Willmar
‡	Wagner, Norman W.	Benson
‡†	Wilmot, Harold E.	Litchfield

MOWER COUNTY MEDICAL SOCIETY

Mower County
Regular meetings, fourth Friday of the month
Annual meeting, November
Number of members 36

	PRESIDENT	
	Mlinar. Joseph	Austin
	SECRETARY	
	Stahl, George	Austin
‡	Anderson, David P., Jr.	Austin
‡	Anderson, Harold J.	Austin
†‡	Cronwell, Bernhard J.	Austin
‡	Hagen, John D.	Austin
†	Hertel, Garfield E.	McAllen, TX
‡	Hesla, Inman A.	Austin
‡	Isele, Reginald	Austin
	Khan, R. A.	Austin
†	Leck, Paul C.	Palm Desert, CA
‡	Lommen, M. L.	Austin
	Lommen, Peter A., Jr.	Austin
†	McKenna, Jay K.	LaJolla, CA
‡	Miller, Herman	Austin
‡	Mlinar, Joseph P.	Austin
†	Morse, Morton P.	LeRoy
	Morse, Roger D.	LeRoy
‡	Muchow, Gene C.	Austin
‡	O'Rourke, William J.	Austin
‡	Osborn, Donald	Austin
	Patten, John C.	Austin
‡	Pesonen, Clifford A.	Austin
†	Peterson, Stanley C.	Sun City, AZ

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Mower County Medical Society *(Continued)*

‡	Roberts, George A.	Austin
†	Robertson, Paul A.	Austin
†‡	Rosenthal, F. Harold	Austin
	Schindler, Richard	Austin
‡	Seery, Thomas M.	Austin
†	Smythe, Gwendolyn S.	Austin
‡	Smythe, Lowell J.	Austin
‡	Snyder, Clinton F.	Austin
	Stahl, G. W.	Austin
‡	Taufic, Mansur	Austin
†	Thomson, James M.	St. Paul
‡	Twiggs, Leo F.	Austin
‡	Van Cleve, H. P., Jr.	Austin
‡	Wright, Robert R.	Austin

NICOLLET-LeSUEUR COUNTY MEDICAL SOCIETY

Nicollet and LeSueur Counties
Regular meetings, first Monday of even months
Annual meeting, December
Number of members 20

	PRESIDENT	
	Sheppard, Charles	LeSueur
	SECRETARY	
	Walden, A. Don	LeSueur
‡	Anderson, Jo E.	LeSueur
	Brink, Donald	St. Peter
‡	Engstrom, George E.	St. Peter
	Granger, Sylvia B.	St. Peter
‡	Grimes, Burton P.	St. Peter
†	Haes, Julius E.	St. Peter
†	Hiniker, Peter J.	St. Peter
†	Larson, Milo H.	St. Peter
†	Lenander, Mellvin E. L.	St. Peter
*‡	Olmanson, Edmund G.	St. Peter
‡	Olmanson, M. Donald	St. Peter
‡	Olmanson, Vern	St. Peter
	Reischl, Elizabeth K.	St. Peter
‡	Sheppard, Charles G.	St. Peter
†	Sjostrom, Lawrence E.	St. Peter
	Sonnesyn, Nels N.	LeSueur
‡	Stolee, Curtis N.	St. Peter
‡	Strathern, Carleton S.	St. Peter
	Thompson, A. Henry	St. Peter
‡	Walden, A. Don	LeSueur
†	Wohlrabe, Clarence F.	North Mankato

PARK REGION DISTRICT AND COUNTY MEDICAL SOCIETY

Douglas, Grant, Otter Tail and Wilkin Counties
Regular meetings, March, June, September and December
Annual meeting, December
Number of members 69

	PRESIDENT	
	Perkins, D. E.	Alexandria
	SECRETARY	
	Engebretson, Paul	Alexandria
	Akhavan, Traz H.	Alexandria
†	Arndt, Harry W.	Detroit Lakes
	Baker, Jeannette L.	Fergus Falls
‡	Barnes, M. J.	Battle Lake
‡	Bateman, Clarence V.	Fergus Falls
	Cain, James H.	Alexandria
	Carlson, C. E.	Alexandria
‡	Carlson, Homer J.	Pelican Rapids
*	Clifford, George W.	Alexandria
‡	Colman, Edward L.	Fergus Falls
‡	Daehlin, Rolf	Fergus Falls
‡	Doms, Vernon A.	Elbow Lake
	Emerson, Edwin E.	Osakis
	Engebretson, Paul	Alexandria
‡	Estrem, Ralph L.	Fergus Falls
‡	Estrem, Robert D.	Fergus Falls
‡	Frerichs, Roger L.	Fergus Falls
	Geiser, Peter M.	Alexandria
	Green, John F.	Alexandria
†	Hanson, Everett C.	New York Mills
‡	Heegaard, William G.	Alexandria
†‡	Helseth, Hovald K.	Fergus Falls
	Henry, Stephen	Alexandria
‡	Hom, Leong Y. W.	Fergus Falls
†	Houkom, Bjarne	Grants Pass, OR
‡	Hunt, Kai K.	Alexandria
‡	Jacobson, Clifford W.	Breckenridge
	Jantunen, K.	New York Mills
‡	Kevern, Jay L.	Henning
‡	Kippen, Neil	Breckenridge
‡	Korda, Henry A.	Pelican Rapids
	Kuhlmann, Vernon G.	Alexandria
	Larson, Dorette W.	Fergus Falls
‡	Lewis, Charles W.	Henning
	Lindley, Stanley B.	Fergus Falls
	Lu, Cheng-en	Fergus Falls
	Lu, Jenning W. G.	Fergus Falls
‡	Luh, Edwin F.	Fergus Falls
‡	Mathison, Larry A.	Fergus Falls
	Merickel, Joseph	Alexandria
‡	Mouritsen, Glenn J.	Fergus Falls
	Myhre, John H.	Fergus Falls
	Nelson, Roy A.	Fergus Falls
‡	Ness, Richard A.	Fergus Falls
	Nicholson, Richard W.	Fergus Falls
†	Olson, Frances P.	Fergus Falls
‡	O'Brien, Louis T.	Breckenridge
‡	Orandi, Ahmad	Fergus Falls
‡	Orandi, Mehdi	Fergus Falls
†	Ostergaard, Erling	Elbow Lake
†	Parson E. Lillian B.	Elbow Lake
‡	Pearson, J. W.	Fergus Falls
	Perkins, Douglass E.	Alexandria
‡	Pulido, Ernesto	Fergus Falls
	Reinhardt, James H.	Alexandria
‡	Richter, Paul H.	Fergus Falls
‡	Rockwood, Philo H.	Fergus Falls
‡	Sanderson, David J.	Fergus Falls
	Schoeneberger, P. B.	Perham
‡	Shaver, Ward	Fergus Falls
	Solien, Arlip	Alexandria
‡	Stemsrud, Harold L.	Alexandria
	Struthers, Lewis	Parkers Prairie
‡	Syverson, Leslie A.	Fergus Falls
†	Tanquist, Edwin J.	Alexandria
	Tanquist, Edwin J., Jr.	Alexandria
	Thompson, Michael	Alexandria
‡	Trajano, Lorenzo F.	Fergus Falls
	Undem, Dale	Alexandria
	Wasson, Loren F.	Alexandria

RAMSEY COUNTY MEDICAL SOCIETY

Ramsey County
Regular meetings, last Monday each month except
June, July and August
Annual meeting in January
Number of members 693

	PRESIDENT	
	Flom, Robert S.	St. Paul
	SECRETARY	
	England, Rodney	St. Paul
	EXECUTIVE SECRETARY	
	Aldean, Mrs. Sue	St. Paul
	Abrams, Alexander, Jr.	St. Paul
	Adair, Albert F., Jr.	St. Paul
	Adams, Harold R.	St. Paul
	Adcock, Leon L.	Minneapolis
	Adcock, Madeline S.	St. Paul
	Ahlstrom, Robert C.	St. Paul
‡	Ahrens, Robert M.	St. Paul
‡	Alden, John F.	St. Paul
	Allan, James W.	St. Paul
	Altman, Robert L.	St. Paul
‡	Alton, Donald G.	St. Paul
‡	Amerongen, Werner W.	St. Paul
‡	Anderson, Dale L.	St. Paul
‡	Anderson, David W.	St. Paul
‡	Anderson, James J.	St. Paul
	Anderson, Margaret C.	St. Paul
‡	Anderson, Richard W.	St. Paul
‡	Antolak, Stanley J., Jr.	St. Paul
‡	Arnold, Neil I.	St. Paul
	Arnold, Patrick N.	St. Paul
‡	Arny, Frederick D.	St. Paul
†	Arny, Frederick P.	St. Paul
‡	Arny, Peter D.	St. Paul
	Ashmore, Herbert C.	St. Paul
	Asp, Donald S.	St. Paul
‡	Ault, Lynn L.	St. Paul
‡	Auran, David B.	St. Paul
‡	Aurelius, J. Richards	St. Paul
‡	Ausman, Duane R.	St. Paul
‡	Austrian, Sol	St. Paul
‡	Baab, Gary H.	St. Paul
‡	Babb, Frank S.	St. Paul
	Bach, Jerome M.	Minneapolis
‡	Bagnoli, Thomas C.	Minneapolis
‡	Bah, Merle C.	St. Paul
‡	Bailey, Walter L.	St. Paul
‡	Baker, C. Robert, Jr.	St. Paul
‡	Balce, Regino V.	St. Paul
	Bauer, Eugene L.	St. Paul
‡	Beck, Charles J.	North St. Paul
	Beckman, Donovan L.	St. Paul
‡	Beek, Harvey O.	St. Paul
‡	Beer, John J.	St. Paul
‡	Bellomo, James	St. Paul
	Belsito, Alphonso A.	St. Paul
‡	Belz, Reinmar	St. Paul
	Bennington, Judith A.	Chaska
‡	Bergh, Allen V.	St. Paul
‡	Bergstedt, John E., Jr.	St. Paul
‡	Bernier, M. J.	St. Paul
†	Bernstein, William C.	St. Paul
‡	Bieter, Thomas G.	St. Paul
	Birkebak, Roland C.	St. Paul
	Bjornson, Robert G. B.	St. Paul
	Blackburn, Henry W.	Minneapolis
‡	Blomberg, William R.	St. Paul

	Blumberg, Henry B.	St. Paul
†	Bock, Rolland A.	St. Paul
	Boies, Lawrence R., Jr.	St. Paul
	Bonello, Frank J.	St. Paul
‡	Bosch, Otto K.	St. Paul
†	Bouma, Lewis R.	St. Paul
‡	Brainard, John B.	St. Paul
	Brandt, Donald E.	St. Paul
	Breen, John J.	St. Paul
‡	Brennom, William S.	St. Paul
	Briggs, Thomas G.	White Bear Lake
	Broadie, Thomas A.	Minneapolis
	Broadie, Thomas E.	St. Paul
	Brockberg, Daryl G.	St. Paul
£‡	Brockberg, James A.	St. Paul
†	Brodie, Walter D.	St. Paul
‡	Broman, Harold R., Jr.	North St. Paul
	Brown, Charles T.	St. Paul
‡	Brown, Christopher J.	St. Paul
‡	Brown, Hector M.	St. Paul
‡	Brown, James E., Jr.	St. Paul
‡	Brown, James P.	St. Paul
‡	Brown, John M.	St. Paul
‡	Bruhl, Martin G.	St. Paul
‡	Bulinski, Theodore J.	St. Paul
‡	Burklund, Edwin C.	St. Paul
	Burlingame, David A.	St. Paul
‡	Burns, John M.	St. Paul
£	Burns, Sheldon	St. Paul
‡	Burton, J. Richard	St. Paul
‡	Bush, Robert P.	St. Paul
	Bustos, Manuel	St. Paul
‡	Butler, Brooks A.	St. Paul
	Butwinick, Conrad S.	St. Paul
	Byrne, William J.	St. Paul
‡	Cain, Clark L.	St. Paul
‡	Campion, Brian C., Jr.	St. Paul
‡	Canto, Jose D.	St. Paul
‡	Capistrant, Terrance D.	St. Paul
‡	Carley, Richard B.	St. Paul
	Cass, Alexander S.	St. Paul
	Cass, Irene D.	St. Paul
‡	Cassell, Wilfred	St. Paul
	Cedarleaf, Cherry B.	White Bear Lake
*†	Chatterton, Carl C.	St. Paul
	Chilgren, Keith V.	St. Paul
‡	Chua, Marianito S.	White Bear Lake
	Clark, W. Bruce	St. Paul
	Cleary, John	St. Paul
‡	Cochrane, Byron B.	St. Paul
	Coddon, Walter D.	St. Paul
†	Colby, Woodward L.	St. Paul
*	Cole, Wallace H.	St. Paul
‡	Coleman, John B.	St. Paul
‡	Colton, Roger S.	St. Paul
‡	Comfort, Thomas H.	St. Paul
‡	Connolly, Coleman J.	St. Paul
‡	Connolly, Joseph P.	South St. Paul
†	Connor, Charles E.	St. Paul
	Cooper, Charles C.	Moose Lake
	Cooper, Jack M.	St. Paul

Ramsey County Medical Society *(Continued)*

‡	Craig, David M.	St. Paul
‡	Cram, Barclay M.	St. Paul
‡	Cramer, Glen G.	New Brighton
	Crowley, James H.	St. Paul
‡	Crudo, Vincent D.	St. Paul
‡	Crum, Arthur Z.	St. Paul
‡	Crutchfield, Charles E.	St. Paul
	Crutchfield, Susan E.	St. Paul
‡	Culligan, David E.	St. Paul
‡	Culligan, John A.	St. Paul
*†‡	Culver, Lucian G.	St. Paul
‡	Cumming, Edward D.	St. Paul
‡	Daly, Alfred E.	St. Paul
‡	Damberg, Sheldon W.	St. Paul
	Davis, Edward V.	St. Paul
	Davis, Eunice R. A.	St. Paul
£	Davis, William E.	St. Paul
	DeCubas, Luis A.	St. Paul
‡	Derauf, Donald E.	St. Paul
‡	Derechin, William	St. Paul
	Derro, Robert A.	St. Paul
‡	Deters, Donald C.	St. Paul
‡	Dickinson, Paul B.	St. Paul
‡	Dieperink, Willem	St. Paul
†‡	Dittrich, Raymond J.	St. Paul
	Dolmage, George H.	St. Paul
§	Domino, Terry	St. Paul
‡	Dooley, Robert T.	St. Paul
	Drydal, Paul J.	St. Paul
	Duerr, Eleanor E.	St. Paul
‡	Duffy, John L.	St. Paul
‡	Dunham, Charles K.	St. Paul
‡	Dunn, James P.	St. Paul
	Dunn, Robert C.	St. Paul
‡	Durkin, John L.	St. Paul
‡	Duthoy, Everette J.	St. Paul
	Dutt, Raj	St. Paul
‡	Duvall, Arndt J., III	St. Paul
‡	Earl, John R.	St. Paul
†	Edwards, J. Willard	St. Paul
‡	Edwards, Jesse E.	St. Paul
	Edwards, Laura E.	St. Paul
	Edwards, Lloyd G.	St. Paul
	Edwards, Thomas J.	St. Paul
	Edwardson, Phillip L.	St. Paul
‡	Eelkema, Herman H.	St. Paul
	Eginton, Charles T.	Fargo, ND
‡	Eilers, Vincent E.	St. Paul
	Ellis, Ronald W.	St. Paul
‡	Elumba, Teodoro V.	St. Paul
†	Emerson, Edward C.	St. Paul
‡	Emmons, Robert W.	St. Paul
*†	Endress, Edward K.	St. Paul
‡	England, Rodney W.	St. Paul
‡	Enroth, Oscar E.	St. Paul
	Erickson, Donald L.	St. Paul
	Erlanson, A. Cornell	St. Paul
	Erling, Carl B.	St. Paul
‡	Ersfeld, Murray P.	St. Paul
‡	Farr, John D.	St. Paul
‡	Fee, John G.	St. Paul
‡	Felder, Davitt A.	St. Paul
‡	Felion, Arthur J.	St. Paul
†	Fesler, Harold H.	West St. Paul
‡	Fink, Daniel L.	St. Paul
‡	Fischer, Robert F.	St. Paul
‡	Flannery, Hubert F.	St. Paul
	Fleming, Janice L.	St. Paul
	Flom, Reynold P.	St. Paul
‡	Flom, Robert S.	St. Paul
‡	Flynn, Louis L., Jr.	St. Paul
*†‡	Fogelberg, Emil J.	St. Paul
‡	Foreman, Richard T.	St. Paul
	Forsythe, James R.	St. Paul
	Fox, LeRoy J.	St. Paul
‡	Freeman, Charles D., Jr.	St. Paul
	Fritz, Wallace L.	St. Paul
£	Froehling, Rodney C.	Minneapolis
	Frost, John W.	St. Paul
£	Fruen, Paul R.	St. Paul
‡	Frye, Charles W.	St. Paul
‡	Fuller, Benjamin F.	White Bear Lake
	Funke, Joyce L.	St. Paul
‡	Gaertner, Frank M. J., Jr.	St. Paul
‡	Gaertner, John R.	St. Paul
	Gaither, Daniel W.	St. Paul
	Galejs, Aina	St. Paul
‡	Galligan, John J.	St. Paul
‡	Gardner, Walter P.	St. Paul
*†	Garrow, Douglas M.	St. Paul
	Gaute, Svend T.	St. Paul
‡	Gedgaudas, Eugene	St. Paul
†	Gehlen, Joseph N.	St. Paul
‡	Geist, Robert W.	St. Paul
	Gibbs, Edward C.	St. Paul
	Gilbertson, David L.	St. Paul
‡	Gilchrist, Milton R.	St. Paul
‡	Gillespie, Delmar R.	St. Paul
	Gillespie, Malcolm E.	St. Paul
‡	Gilsdorf, Donald A.	St. Paul
‡	Glenny, William R.	St. Paul
	Goldsmith, Joseph W.	St. Paul
	Goodman, Ernest	St. Paul
‡	Goott, Bernard	St. Paul
†	Govrik, Kalman	St. Paul
	Graham, Richard S.	St. Paul
‡	Gretsch, Gerald A.	St. Paul
	Gridley, John W.	St. Paul
‡	Griffin, Patrick J.	St. Paul
‡	Gudio, Felix A., Jr.	St. Paul
‡	Guiton, Carl R.	St. Paul
‡	Gumnit, Robert J.	St. Paul
	Guthrie, J. Cameron	St. Paul
	Guthrie, Richard B.	Minneapolis
£	Haemmerle, James H.	St. Paul
‡	Haight, James W.	St. Paul
	Hakanson, Erick Y.	St. Paul
‡	Hall, Barnard	St. Paul
‡	Hammes, Ernest M., Jr.	St. Paul
	Hannon, Donald W.	St. Paul
‡	Hanton, Edward M.	St. Paul
	Harmon, Gaius E.	St. Paul
	Harris, Boyd L.	St. Paul
‡	Harris, John E.	Minneapolis
‡	Harris, Max E.	St. Paul
†	Hartfield, William F.	St. Paul
	Hartig, Marjorie	St. Paul
	Haus, Erhard	St. Paul
‡	Hauser, Charles W.	St. Paul
†‡	Hauser, Victor P.	St. Paul
	Hauser, W. Allen	St. Paul
‡	Hawkinson, Harlan W.	St. Paul
‡	Hayes, Albert F.	St. Paul
†‡	Heck, William W.	St. Paul
‡	Hedenstrom, Charles W.	St. Paul
*†	Hedenstrom, Frank G.	St. Paul
‡	Hedenstrom, Richard H.	St. Paul
*†	Hedlund, Charles J.	St. Paul

(Continued on next page)

Ramsey County Medical Society *(Continued)*

Heimel, Albert J. ....St. Paul
‡ Henderson, Terrance P. ....White Bear Lake
‡ Hendrickson, John M. ....St. Paul
† Hengstler, William H. ....St. Paul
Hengel, James A. ....St. Paul
Henke, Clarence E. ....St. Paul
‡ Henke, Wilbert J. ....St. Paul
‡ Henry, James S. ....St. Paul
† Herman, Samuel M. ....Ft. Lauderdale, FL
‡ Herrick, Donald W. ....St. Paul
£ Heuer, Marvin A. ....Inver Grove Heights
‡ Hilger, Jerome A. ....St. Paul
‡ Hilger, Laurence D. ....St. Paul
Hilgers, Robert D. ....Tenafly, NJ
Hilker, Marcus D. ....St. Paul
Hill, Charlotte W. ....St. Paul
£ Hill, Daniel E. ....St. Paul
Hinckley, Robert G. ....White Bear Lake
† Hiniker, Louis P. ....St. Paul
‡ Hippchen, Ray C. ....St. Paul
‡ Hodgson, Corrin H. ....St. Paul
Hodgson, Jane E. ....St. Paul
‡ Hohmann, Albert ....St. Paul
Hollinshead, William H. ....St. Paul
Holmen, Douglas J. ....St. Paul
†‡ Holt, John E. ....St. Paul
Hopkins, G. Wendell ....Minneapolis
‡ Hottinger, George C. ....St. Paul
Houle, Rollin J. ....St. Paul
Houlton, William H. ....St. Paul
Howard, Malin L. ....Wurtsmith AFB, MI
Howe, Newell W. ....West St. Paul
‡ Hunt, Vincent R. ....Minneapolis
Hunter, David L. ....St. Paul
‡ Hunter, Samuel W. ....St. Paul
‡ Hurwitz, Milton M. ....St. Paul
‡ Huseby, Thomas L. ....St. Paul
‡ Husebye, Kjeld O. ....St. Paul
Indehar, Frank J. ....St. Paul
Ireland, Gerald W. ....Napa, CA
‡ Jackson, William C. ....St. Paul
‡ James, Ellery M. ....St. Paul
§ James, Ellery M., II ....Mahtomedi
‡ James, John W. ....St. Paul
‡ Janecek, James ....New Brighton
‡ Janssen, Martin E. ....St. Paul
Jarvis, Charles W. ....St. Paul
‡ Jastram, Rupert M. ....St. Paul
Johnson, Byron R. ....St. Paul
Johnson, Carl E. ....St. Paul
Johnson, Carolyn A. ....St. Paul
‡ Johnson, Daniel T. ....St. Paul
£‡ Johnson, David W. .... St. Paul
‡ Johnson, Herbert W. ....St. Paul
#‡ Johnson, Lyle O. ....St. Paul
‡ Johnson, Richard J. ....St. Paul
‡ Johnson, Robert H. ....St. Paul
‡ Johnson, Rodger L. ....St. Paul
Johnson, Stanley M. ....White Bear Lake
‡ Johnson, Thomas E. ....St. Paul
Joseph, Arnold H. ....St. Paul
‡ Kantar, Yale C. ....St. Paul
Kaplan, David H. ....Edina
‡ Kapps, F. Donald ....St. Paul
Karon, Everett H. ....St. Paul
‡ Karon, Irvine M. ....St. Paul
‡ Kasper, Eugene M. ....St. Paul
Keenan, Thomas P. ....St. Paul
‡ Keller, Curtis ....White Bear Lake
Kelly, Edward H. ....St. Paul
Kelly, Helen M. ....Cottage Grove
‡ Kelly, Joseph R. ....St. Paul
‡ Kelsey, Chauncey M. ....St. Paul
‡ Kenyon, Thomas J. ....St. Paul
† Kesting, Herman ....St. Paul
Kiernan, John H. ....St. Paul
Kjellstrand, Carl M. ....Minneapolis
Kleinsasser, Warren L. ....St. Paul
Kluge, John W. ....St. Paul
‡ Knowles, Roy C. ....St. Paul
‡ Knutson, Gerhard E. ....St. Paul
Knutson, Robert C. ....St. Paul
Kodres, Nina ....St. Paul
Koelz, Thomas A. ....St. Paul
‡ Kosiak, Michael ....St. Paul
£‡ Kovacs, J. Curtis ....St. Paul
Koza, Donald W. ....St. Paul
‡ Kramer, James D. ....St. Paul
‡ Krasnow, Brian M. ....Minneapolis
‡ Krezowski, Thomas K. ....St. Paul
Kriel, Robert L. ....St. Paul
Kugler, Alex A. ....St. Paul
‡ Kuske, Albert W. ....St. Paul
‡ Kusske, Bradley W. ....St. Paul
‡ Kusske, Douglas R. ....St. Paul
‡ Kvam, Lowell L. ....St. Paul
Lade, Roswith I. ....St. Paul
‡ LaFave, James W. ....St. Paul
LaKosky, Randall ....St. Peter
Lampert, Ronald M. ....St. Paul
‡ Lane, Miles I. ....White Bear Lake
‡ Lannin, Bernard G. ....St. Paul
‡ Lannin, Donald R. ....St. Paul
Larkin, John E. ....St. Paul
‡ Larson, Bert W. ....St. Paul
Larson, Eva Jane Ostergren ....St. Paul
‡ Larson, Jerrold V. ....St. Paul
† Laszewski, Franz Von Zelberschwecht ....St. Paul
‡ Lawler, Kevin M. ....St. Paul
Layman, Thomas E. ....St. Paul
‡ Leach, Clifford G. ....St. Paul
Leahy, Dennis M. ....St. Paul
‡ Lees, Jack R. ....St. Paul
Lehman, Donald S. ....St. Paul
‡ Leick, Richard M. ....St. Paul
‡ Leider, Lloyd L. ....St. Paul
† Leitch, Archibald ....South St. Paul
‡ Leonard, Stanley ....St. Paul
‡ Lerdahl, Kenneth ....St. Paul
‡ Lerner, Irving, J. ....St. Paul
Lessard, Richard J. ....St. Paul
† Leven, N. Logan ....St. Paul
‡ Leverenz, Carleton W. ....St. Paul
‡ Levitan, Leonard H. ....St. Paul
Levitt, George X. ....St. Paul
Lewis, Joyce S., Jr. ....Minneapolis
‡ Lick, William J. ....St. Paul
‡ Lien, Richard J. ....St. Paul
† Lightbourn, Edgar L. ....Hastings
‡ Lilleberg, Norbert J. ....St. Paul
‡ Lillemoen, Roger D. ....Minneapolis
Lillie, Andrew R. ....St. Paul
‡ Lindell, Robert E. ....St. Paul
‡ Lindquist, Max F. ....South St. Paul
*† Litkewitsch, Helene ....St. Paul
‡ Lobell, Michael ....St. Paul
‡ Loken, Selmer M. ....St. Paul
‡ Love, Thomas A. ....St. Paul
Lowe, Alexander D. ....West St. Paul
† Lowe, Thomas A. ....South St. Paul

Ramsey County Medical Society *(Continued)*

‡	Lufkin, Murray W.	St. Paul
†‡	Lundholm, Arthur M.	Princeton
‡	Lunseth, John B.	St. Paul
‡	Lunzer, Richard G.	St. Paul
	Lutter, Lowell D.	St. Paul
‡	Lynch, Francis W.	St. Paul
‡	Lynch, Raymond P.	St. Paul
‡	Lynch, Richard P.	St. Paul
‡	McBride, John W.	St. Paul
‡	McCafferty, Charles W.	St. Paul
	McCain, Donovan L.	St. Paul
‡	McCarthy, Charles J.	St. Paul
	McClellan, Robert J.	St. Paul
	McCloud, C. Naumann	St. Paul
	McCullough, Jeffrey J.	St. Paul
‡	McEllistrem, Edward J.	St. Paul
‡	McEllistrem, Gerald D.	St. Paul
‡	McEwan, Alexander	St. Paul
‡	McGroarty, Brian J.	St. Paul
‡	McHutchison, Samuel K.	St. Paul
	McKenzie, Eva E.	St. Paul
	McLeod, John A.	St. Paul
‡	McNeill, John A.	St. Paul
	Mackoff, Sam M.	Phoenix, AZ
	MacMillan, David G.	St. Paul
†	Madland, Robert S.	St. Paul
‡	Maher, Thomas D.	St. Paul
‡	Malerich, J. Anthony, Jr.	Cottage Grove
‡	Manlove, Charles H., Jr.	St. Paul
‡	Marta, John B.	St. Paul
‡	Martin, Dwight L.	St. Paul
	Mateo, Guillermo	St. Paul
	Matthews, Marilyn L.	St. Paul
	Matus, Richard N.	St. Paul
	Mazzitello, William F.	St. Paul
‡	Mears, Burtis J.	St. Paul
‡	Medelman, John P.	St. Paul
‡	Melancon, Joseph F.	St. Paul
‡	Merrick, Robert L.	St. Paul
‡	Messenger, Michael A.	St. Paul
‡	Michienzi, Leonard J.	St. Paul
‡	Miller, Albert G.	St. Paul
‡	Miller, Fletcher A.	St. Paul
	Miller, Winston R.	St. Paul
	Miller, Zondal R.	St. Paul
‡	Milnar, Frank J.	St. Paul
	Mishek, Charles J.	St. Paul
‡	Mitchell, George S.	St. Paul
†	Molander, Herbert A.	St. Paul
	Molina, J. Ernesto	St. Paul
‡	Moller, Jurgen J.	West St. Paul
‡	Monahan, Robert H.	St. Paul
	Mooney, Robert D.	St. Paul
£	Moran, John A.	St. Paul
	Moren, J. Adelaide	St. Paul
‡	Mowlem, Albert	St. Paul
	Mulford, Beatrice	St. Paul
‡	Mulhausen, Robert O.	St. Paul
‡	Muller, A. Eugene	North St. Paul
	Mulrooney, Thomas F.	St. Paul
	Mundahl, Harold R.	St. Paul
	Murphy, Jack T.	St. Paul
£	Murtaugh, Robert J.	St. Paul
‡	Myaya, Po	St. Paul
‡	Neher, Frederick J.	St. Paul
‡	Neira, Edward H.	St. Paul
‡	Nelms, Charles R. Jr.	St. Paul
£‡	Nelson, David J.	St. Paul
‡	Nelson, Delbert R.	St. Paul
‡	Nelson, Loren E.	St. Paul
‡	Nelson, Louis A.	St. Paul
‡	Nelson, Robert P.	St. Paul
‡	Nelson, Ronald J.	St. Paul
	Nesvacil, Leon	St. Paul
‡	Nichols, Thomas O.	St. Paul
£	Nimlos, Kenneth O.	St. Paul
£	Nimlos, Lenore O.	St. Paul
‡	Norman, David D.	St. Paul
	Norquist, Joseph L.	St. Paul
	O'Brien, Gerald R.	Minneapolis
‡	O'Brien, John C.	St. Paul
‡	O'Kane, Thomas W.	St. Paul
‡	O'Malley, Valentine	St. Paul
‡	O'Neill, Nial C.	St. Paul
†	O'Reilley, Bernard E.	Sun City, AZ
	Ockuly, Orville E.	St. Paul
†	Ogden, Warner	River Falls, WI
†	Ohage, Justus	St. Paul
‡	Olsen, Ralph L.	St. Paul
	Olson, Barbara F.	Minneapolis
‡	Orr, Ernest W.	St. Paul
‡	Osekowsky, Henry J.	St. Paul
†‡	Ouellette, Alfred	St. Paul
‡	Owens, Frederick M., Jr.	St. Paul
	Padilla, Cerfenio B., Jr.	St. Paul
‡	Palm, Neil M.	St. Paul
	Pangalos, Anastase	St. Paul
‡	Paulson, Elmer C.	St. Paul
‡	Paulson, Wallace J.	St. Paul
	Peake, Janna Zoe	St. Paul
†	Pearson, Fritz R.	St. Paul
‡	Pearson, Malcolm M.	St. Paul
†	Pedersen, Arthur H.	St. Paul
‡	Pelletier, Rene W.	St. Paul
‡	Perry, John F., Jr.	St. Paul
£	Petersen, Kenneth	Portland, OR
‡	Peterson, Donald H.	St. Paul
‡	Peterson, Edward A.	St. Paul
£	Peterson, Garry F.	St. Paul
‡	Peterson, Harold O.	Minneapolis
£	Peterson, Lance R.	Minneapolis
£	Peterson, LoAnn	Minneapolis
‡	Peterson, Roy L.	White Bear Lake
	Phillips, Leonard	St. Paul
‡	Pilney, Frank T.	St. Paul
‡	Pitzele, Charles E.	St. Paul
	Plotke, Harry L.	St. Paul
‡	Polga, James P.	St. Paul
	Polski, Paul G.	South St. Paul
‡	Post, Edmund A.	St. Paul
‡	Powers, Robert L.	St. Paul
‡	Proud, Harry S.	St. Paul
‡	Quast, John E.	St. Paul
	Quattlebaum, Frank W.	St. Paul
‡	Raaen, Olaf J.	St. Paul
	Rabcevich, Anatole	St. Paul
£	Rafferty, Dwight K.	St. Paul
‡	Ralph, James R.	St. Paul
	Ramirez-Lassepos, Manuel	St. Paul
	Ramlow, Ralph M.	West St. Paul
‡	Raths, Otto N., Jr.	St. Paul
‡	Rauenhorst, John M.	St. Paul
‡	Ravits, Harold G.	St. Paul
‡	Rea, Charles E.	St. Paul
	Redleaf, Paul D.	St. Paul
	Reif, Robert W.	St. Paul
‡	Richardson, Edward J., Jr.	St. Paul
‡	Rick, Paul F. W.	St. Paul

(Continued on next page)

Ramsey County Medical Society *(Continued)*

£	Rigatuso, Joseph L.	St. Paul
‡	Rinkey, Eugene	St. Paul
†	Ripple, Rudolph J.	St. Paul
†‡	Ritt, Albert E.	St. Paul
‡	Roach, Charles A.	St. Paul
‡	Roach, Donald E.	St. Paul
£	Rodning, Charles B.	St. Paul
*‡	Rolig, David H.	West St. Paul
	Romero, Jose B.	St. Paul
†‡	Rosenthal, Robert	St. Paul
‡	Rowe, Clarence J., Jr.	St. Paul
‡	Roy, Philemon C.	St. Paul
‡	Roy, Philamon C. Jr.	St. Paul
‡	Rukavina, John G.	St. Paul
‡	Rushay, Arthur J.	White Bear Lake
‡	Rusterholz, Alan P.	St. Paul
†‡	Ryan, John J.	St. Paul
‡	Ryan, Joseph M.	St. Paul
‡	Sand, Richard E.	St. Paul
‡	Savett, Laurence A.	St. Paul
	Saxena, Krishna M.	St. Paul
	Saxena, Kusum	St. Paul
	Scanlan, John M.	St. Paul
‡	Schaffhausen, George E.	St. Paul
‡	Scherek, Jerome J.	St. Paul
‡	Schloff, Ivan	St. Paul
	Schloff, Leonard D.	St. Paul
	Schmidtke, Reinhardt L.	Minneapolis
‡	Schochet, H. Laurence	St. Paul
	Schoewe, Richard W.	Minneapolis
†	Schons, Edward	Minnetonka Beach
‡	Schossow, George W.	White Bear Lake
‡	Schroeckenstein, Hugo F.	St. Paul
‡	Schultz, Paul E.	St. Paul
	Schwartz, Carl E.	St. Paul
	Schwartzkopff, Othild	St. Paul
‡	Scott, Eugene E.	St. Paul
	Sekhon, Mohan S.	St. Paul
‡	Sells, Richard J.	St. Paul
‡	Sethre, Arthur E.	St. Paul
†‡	Setzer, Hobert J.	St. Paul
£	Shah, Ranjana N.	Minneapolis
†	Shannon, William R.	Minneapolis
	Shear, Howard H.	West St. Paul
‡	Shelander, Marcus I.	St. Paul
	Siegel, Clarence	W. Palm Beach, FL
‡	Siegel, Leighton G.	St. Paul
	Simmonds, Harry N. L.	St. Paul
‡	Simons, Leander T.	St. Paul
‡	Singer, Benjamin J.	St. Paul
‡	Skelly, George A.	St. Paul
‡	Skinner, Abbott	St. Paul
†	Skinner, Harvey O.	St. Paul
‡	Smiley, Donald P.	St. Paul
†‡	Smisek, Elmer A.	St. Paul
‡	Smith, H. Nippert	St. Paul
£	Smith, James C.	St. Paul
‡	Smith, Vernon D. E.	St. Paul
‡	Smith, William T.	St. Paul
‡	Smookler, Richard	St. Paul
†	Snyder, George W.	St. Paul
†	Sohlberg, Olof I.	St. Paul
‡	Sommerdorf, Vernon L.	St. Paul
	Sorem, Milton B.	St. Paul
‡	Soucheray, John A.	St. Paul
†‡	Souster, Benjamin B.	St. Paul
	Sowada, Dorothea Pollock	St. Paul
	Sowada, Ernest	St. Paul
‡	Sperl, Michael P., Jr.	St. Paul
	Sprafka, Gregory A.	St. Paul
‡	Sprafka, Joseph L.	St. Paul
‡	Spraitz, Anton F., Jr.	St. Paul
‡	Stafne, John G.	St. Paul
‡	Steinberg, Charles L.	St. Paul
‡	Sterner, Donald C.	St. Paul
‡	Sterner, John J.	St. Paul
	Strate, Richard G.	St. Paul
	Straus, Maurice L.	St. Paul
‡	Strem, Edward L.	St. Paul
‡	Sturley, Rodney F.	St. Paul
	Sullivan, Cornelius	St. Paul
‡	Sullivan, W. Albert, Jr.	St. Paul
‡	Swanson, Lawrence J.	West St. Paul
‡	Swanson, Ralph H.	West St. Paul
	Swayze, Claude R.	St. Paul
†	Swendson, James J.	St. Paul
‡	Swenson, Donald B.	St. Paul
	Syong, Matilde	St. Paul
‡	Taddeini, Luigi	St. Paul
‡	Tanasichuk, Murray A.	St. Paul
‡	Tani, George	St. Paul
‡	Tate, Wayne E.	South St. Paul
*‡	Teeter, Richard R.	St. Paul
‡	Teisberg, John E.	St. Paul
‡	Thalhuber, Wayne H.	St. Paul
‡	Thompson, Wayne W.	St. Paul
	Tiffany, Francis B.	St. Paul
‡	Tifft, Cyril R.	St. Paul
‡	Tongen, Lyle A.	St. Paul
‡	Travis, James S.	St. Paul
	Tregilgas, Richard B.	St. Paul
‡	Trotman, Neil M.	St. Paul
‡	Troup, Elliott	St. Paul
	Trow, William H.	St. Paul
‡	Tuason, Vicente B.	St. Paul
	Tveten, Omar A.	St. Paul
‡	Ubel, Frank A.	St. Paul
	Vaccarella, R. James	St. Paul
‡	Van Bergen, Frederick H.	Minneapolis
‡	Van De Riet, Lowell W.	St. Paul
	van Tyn, Robert A.	St. Paul
	Varco, Richard L.	St. Paul
‡	Vaughn, C. Gordon	St. Paul
	Veinbergs, Arnold	St. Paul
*†	Veirs, Dean M.	Hastings
†	Venables, Alexander E.	Marysville, WA
‡	Venters, Homer D., Jr.	St. Paul
	Verwest, Hadley M., Jr.	St. Paul
‡	Villafani, Mario F.	St. Paul
‡	Votel, Thomas W.	St. Paul
†	Waas, Charles W.	St. Paul
‡	Wall, James O.	St. Paul
‡	Walsh, Edward F.	St. Paul
‡	Walsh, William E.	St. Paul
‡	Walter, Clarence W.	St. Paul
	Wang, Helen H.	St. Paul
	Wangsness, Mary S.	St. Paul
‡	Warner, Clyde M.	St. Paul
‡	Warren, Cecil A.	St. Paul
	Waters, Alvin W.	St. Paul
‡	Watson, P. Theodore	St. Paul
‡	Watson, William H. A.	St. Paul
‡	Watson, William J.	Newport
	Watz, Clarence E.	St. Paul
	Webb, Alex G., Jr.	St. Paul
†‡	Webber, Fred L.	St. Paul
‡	Wedes, Deno J.	St. Paul
‡	Weier, Thomas E.	St. Paul

amsey County Medical Society *(Continued)*

	Weisberg, Maurice	St. Paul
	Weiss, Larry W.	St. Paul
	Wenzel, Gilbert P.	St. Paul
	Westover, Darrell E.	St. Paul
	Wetteland, Thomas F.	West St. Paul
	Wetzel, Earl V.	St. Paul
	Whiting, F. Douglas	St. Paul
	Wiencke, William M.	St. Paul
	Wier, G. Thomas	St. Paul
	Wild, John J.	Minneapolis
	Williams, George E.	St. Paul
	Williams, Harry J., III	St. Paul
	Williams, Hugh J.	St. Paul
	Williams, John A.	St. Paul
	Williams, Richard A.	Cottage Grove
‡	Wilson, Fred B.	St. Paul
‡	Winter, Robert B.	St. Paul
	Wolkoff, Hyman J.	St. Paul
‡	Woodburn, Robert L.	St. Paul
‡	Woolfrey, Bertram F.	St. Paul
	YaDeau, Richard E.	St. Paul
	Yost, Elaine Benthack	St. Paul
†	Youngren, Everett R.	St. Paul
‡	Yue, Alexander	Minneapolis
†	Zachman, Leo L.	St. Paul
*	Zagaria, James F.	St. Paul
‡	Zanick, David C.	St. Paul
‡	Zarling, Max E.	St. Paul
	Zdenek, Kalyanaraman A.	St. Paul

RANGE MEDICAL SOCIETY

Koochiching, Itasca and the Northern Portion of St. Louis County
Regular meetings, fourth Tuesday of January, March, May, July, September and November
Annual meeting, January.
Number of members 119

	RESIDENT	
	ope, Hershel B.	Virginia
	ECRETARY	
	eMarais, Lloyd C.	Hibbing
	ORRESPONDING SECRETARY	
	vans, Mrs. Virginia	Hibbing
	Ahola, Kenneth E.	Hibbing
	Alexander, Paul J.	Hibbing
	Anderson, Russell H.	Virginia
	Antonelli, Jordan J.	Rochester
	Antonow, Arthur M.	Virginia
	Avren, Barbara L.	Virginia
	Baich, Velemir M.	Coleraine
	Balderson, Robert P.	Grand Rapids
	Baraga, Anthony R.	Hibbing
	Barnes, Richard E.	Aurora
	Bergen, Richard M.	Grand Rapids
	Bernal, Jorge	Virginia
	Bolz, J. Arnold	Grand Rapids
	Bonner, John L.	Grand Rapids
	Braun, Ohrmundt C.	Grand Rapids
	Campos, Amador C.	Eveleth
	Chermak, Francis G.	Phoenix, AZ
	Ciriacy, Edward W.	Minneapolis
	Coe, Robert O.	Virginia
	Colosey, Frederick J.	Virginia
	Cope, Hershel B.	Virginia
	Coy, Douglas J.	Grand Rapids
	Crow, George M.	International Falls
	Davenport, Jay A.	Virginia
	Decker, Charles W.	Hibbing
	DeMarais, Lloyd C.	Hibbing
	Dobler, Manfred G.	Ely
	Doren, Austin H.	Littlefork
	Drucker, Franklin G.	Bigfork
	Eisenman, Walter	Hibbing
	Engelstad, Wendell P.	Virginia
	Erickson, Vernon D.	Grand Rapids
	Evensta, John B.	Grand Rapids
	Ewens, George B.	Virginia
	Ferrell, Clarence R.	Moose Lake
	Flynn, Bernard F.	Hibbing
	French, Bayard T.	Hibbing
	Friedlieb, Oskar P.	Virginia
	Gerend, Thomas J.	Virginia
	Glomstad, Gary B.	Grand Rapids
	Goodall, David C.	Deer River
	Gorden, A. Marc	International Falls
	Grahek, Jack P.	Ely
‡	Greene, Gordon O.	Hibbing
	Grinley, Andrew V.	Grand Rapids
	Halper, Bernard	Hibbing
	Halverson, Kermit J.	Parkville
	Hansen, Robert E.	Hibbing
†	Heiam, William C.	Cook
	Helwig, Karl L.	Virginia
	Henwood, Wesley C.	Virginia
	Holm, Owen W.	Hibbing
	Ibrahim, George W.	Virginia
£	Iverson, Paul C.	Grand Rapids
†	Jacobson, Clarence	Chisholm
	Johnson, Calvin J.	Grand Rapids
	Johnston, H. Wayne	Virginia
	Kampen, Charles P.	Grand Rapids
‡	Karges, Laurel E.	Grand Rapids
‡	Karish, Louis J.	Grand Rapids
‡	Kelly, Robert T.	Grand Rapids
	Kiesler, Frank	Grand Rapids
	Kishel, Gene F.	Virginia
†	Kotchevar, Frank R.	Sun City, CA
	Kruger, E. Larry	Hallock
	Law, Harrison E.	Virginia
	Leach, Thomas C.	Winsted
	Lee, William C.	Hibbing
	Leino, Walter B. Jr.	Ely
	McClelland, John G.	Virginia
	McKenna, John J.	Virginia
	McKenna, Maurice J.	Grand Rapids
	Martinson, Raymond M.	Virginia
	Mast, Fredric L.	Chisholm
	Miettunen, John B.	Hibbing
	Miks, George M.	Grand Rapids
	Miller, Harry G.	Virginia
	Mock, Charles J.	Virginia
	Moyer, Richard R.	Hibbing
	Mueller, Donald R.	Grand Rapids
‡	Muller, John J.	Hibbing
	Murray, Robert A.	Hibbing
	Neff, Walter S.	Virginia
‡	Nelimark, D. Robert	Virginia
	Nelson, Bernette G.	Ely

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Range Medical Society *(Continued)*

‡	Nollet, Donald J.	Hibbing
	Olson, Richard T.	Virginia
	Owens, Ben P.	Hibbing
	Paciotti, Vincent J.	Hibbing
	Parker, Wilbert H.	Chisholm
	Payne, Richard E.	Virginia
	Person, Duane F.	Virginia
†	Peterson, Edward N.	Virginia
	Prlina, Isaac M.	Virginia
	Rayer, Anthony L.	Babbitt
‡	Reed, Paul	Virginia
	Reynolds, Dermot F.	Hibbing
	Richter, David J.	Virginia
‡	Roth, Albert H.	Deer River
†	Rowles, Everett K.	Laguna Hills, CA
†‡	Salter, Reginald A.	Virginia
	Sanders, Paul S.	Babbit
‡	Schirber, Martin J.	Grand Rapid
	Schweiger, Theodore R.	Hibbin
	Schwinghamer, Thomas G.	El
†	Sher, David A.	Virgini
	Siegel, John S.	Virgini
†	Sisler, Clifford E.	Grand Rapid
	Skumatz, Primus J. Jr.	International Fall
	Stolen, Keith H.	Grand Rapid
	Strouth, Jonas C.	Virgini
	Talsness, Jon M.	International Fall
	Tietz, Charles A.	Virgini
	Walker, Stuart B.	Auror
‡	Walter, Frederick H.	International Fall
	Weir, Matthew J.	Virgini
	Werner, Donald L.	Hoyt Lake
	Wheeler, Gilbert S.	Virgini
	Woodruff, Whitney	Virgini

RED RIVER VALLEY MEDICAL SOCIETY

Kittson, Mahnomen, Marshall, Norman, Pennington,
Polk, Red Lake and Roseau Counties
Regular meetings, quarterly
Annual meeting, December
Number of members 56

	PRESIDENT	
	Jensen, John	Crookston
	SECRETARY	
	Berg, A. M.	Thief River Falls
	Behr, Orlo K.	Crookston
‡	Berg, Arnold M.	Thief River Falls
†	Bratrud, Edward	Alexandria
	Bray, Jerome L.	Thief River Falls
‡	Brown, Glenn W.	Halstad
‡	Carter, Robert G.	Thief River Falls
	Choithani, C. M.	Crookston
	Choithani, H. C.	Crookston
	Clapp, Hubert D.	Crookston
‡	Dagg, Earl	Thief River Falls
	Davidson, Duane J.	Thief River Falls
	Delmore, Jack	Roseau
	Dillenburg, Cyril	Crookston
†	Flancher, Leon H.	Detroit Lakes
†	Foderick, Peter P.	Ada
	Herber, Leo	Thief River Falls
	Hirsh, Stanton	Crookston
	Holmstrom, Carle H.	Warren
	Jensen, John A.	Crookston
	Kinkade, Byron R.	Ada
‡	Klefstad, Lloyd H.	Greenbush
†	Kostick, William R.	Fertile
‡	Larter, Roland	Hallock
	Lloyd, Brian E.	Crookston
†	Loken, Theodore	Ada
†	Lynde, Orrin G.	Los Gatos, CA
‡	Martin, George B.	Thief River Fall
	Mercil C. B.	Mahnome
‡	Mercil, William	Crooksto
	Mersy, David J.	Red Lake Fall
	Montaniel, Necito L.	Crooksto
†	Nelson, Henry E.	Crooksto
†	Oppegaard, C. L.	Scottsdale, A
	Ortego, Pedro R.	Crooksto
‡	Parra, Samuel	Crooksto
‡	Pinsonneault, W. A.	Warre
	Reff, Alan R.	Crooksto
†	Roholt, Christian L.	McIntos
‡	Sather, Edgar L.	Fossto
‡	Sather, George A.	Fossto
‡	Sather, Richard N.	Fossto
	Sather, Russell O.	Crooksto
	Scheuneman, Allen F.	Thief River Fall
	Schnabel, Norma B.	Crooksto
	Schnabel, Robert F.	Crooksto
	Skogerboe, Rudolph	E. Grand Fork
	Stadem, Clifford	Crooksto
	Stewart, Donald E.	Crooksto
£	Taylor, Ross M.	Thief River Fall
	Thorbus, Ruben S.	Karlsta
	Thorsgard, Ernest O.	Thief River Fall
	Uhley, Charles G.	Hopkin
‡	Van Rooy, George T.	Thief River Fall
	Vaugh, Charles R.	Crooksto
	Wendt, Paul	Thief River Fall
	Wikoff, Howard M.	Crooksto

RICE COUNTY MEDICAL SOCIETY

Rice County
Regular meetings, third Tuesday of
January, April, September and November
Annual meeting in November
Number of members 27

PRESIDENT
Buesgens, Ralph H. .... Waterville
SECRETARY
Beaton, J. Gordon .... Northfield

Beaton, J. Gordon .... Northfield
Bruhl, Heinz H. .... Faribault
‡ Buesgens, Ralph H. .... Waterville
Clarke, Dean .... Faribault
Evans, James M. .... Northfield
Faust, John H. .... Northfield
‡ Foni, Iancu F. .... Faribault
† Francis, David W. .... Morristown
Good, Roy H. .... Faribault
‡ Graham, Asa B. .... Faribault
Gutzmann, Bruce F. .... Faribault
Haas, Jack F. .... Northfield
Halvorson, David C. .... Northfield
† Kennedy, George L. .... Faribault
† Kolars, James J. .... Faribault
Meyer, Frederick C. .... Kenyon
Meyer, Richard H. .... Faribault
Meyer, Robert P. .... Faribault
Nickerson, John R. .... Faribault
Orr, Burton A. .... Faribault
*† Rumpf, Carl W. .... Faribault
Rysgaard, George N. .... Northfield
Speckhals, Robert C. .... Faribault
Street, Bernard .... Northfield
‡ Studer, Donald J. .... Faribault
† Traeger, Carl A. .... Faribault
Tuma, Benjamin .... Faribault
Weaver, Paul H. .... Faribault

ST. LOUIS COUNTY MEDICAL SOCIETY

Carlton, Cook, Lake and Southern portion of
St. Louis County
Regular meetings, second Thursday in each month
except July and August
Annual meeting in January
Number of members 216

PRESIDENT
Moyer, J. B. .... Duluth
SECRETARY
Wall, Jack E. .... Duluth
SECRETARY, EXECUTIVE OFFICE
Lundgren, Miss Margaret M. .... Duluth

Aas, Johannes .... Duluth
Aas, Martha A. .... Duluth
‡ Abraham, Arden L. .... Duluth
‡ Ahrens, Curtis F. .... Duluth
‡ Asta, Joseph J. .... Duluth
† Athens, A. G. .... Minnetonka
‡ Atmore, William G. .... Duluth
‡ Aufderheide, Arthur C. .... Duluth
Backus, Byron C. .... Cloquet
Backus, Lloyd B. .... Cloquet
† Backus, Reno W. .... Cloquet
‡ Bagley, Charles M. .... Duluth
Bagley, Elizabeth C. .... Duluth
‡ Bakkila, Henry E. .... Duluth
‡ Balmer, Albert I. .... Duluth
‡ Bartzen, Peter J. .... Duluth
‡ Becker, Frederic T. .... Duluth
‡ Bell, Harry M., Jr. .... Duluth
† Bepko, Marie (Puumala) .... Cloquet
‡ Bergan, Robert O. .... Duluth
†‡ Bianco, Anthony J. .... Duluth
† Bloom, Joseph .... Pompano Beach, FL
‡ Bloom, Stephen L. .... Duluth
Blum, Clifford J. .... Duluth
‡ Boecker, Bernhard .... Duluth
† Boman, Paul G. .... Duluth
‡ Boman, Peter L. .... Duluth
Boyer, Samuel H. .... Duluth
‡ Bray, Philip N. .... Duluth
Bromen, Kenneth A. .... Duluth
‡ Brooker, Warren J. .... Duluth
‡ Brown, Cyrus C., Jr. .... Duluth
† Buckley, R. P. .... Duluth
‡ Budd, Frank W. .... Duluth
‡ Bulluck, Matthew H. .... Duluth
‡ Butler, John K. .... Cloquet
‡ Campaigne, Robert J. .... Duluth
‡ Campbell, Craig W. .... Duluth
‡ Carter, Robert E. .... Duluth
‡ Christensen, Clarence H. .... Duluth
Church, Gerald E. .... Two Harbors
Clark, Elizabeth A. (Mrs. Halbert) .... Duluth
Clifford, Thomas M. .... Silver Bay
‡ Coll, James J. .... Duluth
‡ Collins, Roger T. .... Duluth
Cotton, Gerald E. .... Duluth
‡ Cowan, Gary A. .... Duluth
Cowan, George M. .... Duluth
‡ Cox, Milton J. .... Duluth
‡ Creps, James R. .... Duluth
‡ Cuderman, Bart S. .... Duluth
‡ Dailey, John C. .... Duluth
‡ Davidson, A. Dale .... Duluth
Davis, William .... Moose Lake
‡ Deutsch, Robert J. .... Duluth
† Dickson, Franklin H. .... Proctor
‡ Dobbs, Richard L. .... Duluth
‡ Drexler, Charles J. .... Duluth
‡ Dwyer, John J. .... Duluth
‡ Eckman, Matthew J. .... Duluth
Eckman, Philip F. .... Duluth
‡ Eckman, Philip L. .... Duluth
‡ Eckman, Ralph J. .... Duluth
‡ Ecklund, Carl D. .... Duluth
‡ Emanuel, Karl W. .... Duluth
‡ Engelsgjerd, Gerald L. .... Duluth
Evison, Emerson O. .... Duluth
‡ Fawcett, Keith R. .... Duluth
‡ Feuling, John C. .... Sun City, AZ
‡ Fifield, Malcolm M. .... Duluth
‡ Fisketti, Henry .... Duluth
Frederickson, David L. .... Duluth
‡ Fuller, Josiah .... Duluth

(Continued on next page)

St. Louis County Medical Society *(Continued)*

†‡	Gillespie, Malcolm G.	Duluth
‡	Goldish, Daniel R.	Duluth
‡	Goldish, Robert J.	Duluth
‡	Goldschmidt, Volker	Duluth
‡	Goodnow, William H.	Duluth
‡	Gowan, Lawrence R.	Duluth
‡	Gowan, Lawrence R., Jr.	Duluth
‡	Gower, Walter E.	Duluth
‡	Grohs, William H.	Duluth
	Gronquist, Y. K. J.	Cloquet
‡	Haase, Donald D.	Silver Bay
‡	Haavik, John E.	Duluth
	Halbert, John J.	Duluth
‡	Halliday, Phillip V.	Duluth
	Hanson, Ernest O.	Cloquet
†	Harper, David G.	Duluth
‡	Harrington, Vernon A.	Duluth
‡	Heisel, John G.	Duluth
‡	Hilding, Anderson C.	Duluth
	Hoeg, Dwight C.	Duluth
‡	Hoff, Herbert O.	Duluth
‡	Holt, Glen E.	Duluth
‡	Hood, Roderick P.	Duluth
‡	Houglum, Arvid J.	Duluth
†	Houkom, S. Sverre	Duluth
†	Hutchinson, Henry	Minneapolis
	Irving, Stanley	Duluth
	Jacklin, Alexander J.	Duluth
‡	Jacobson, Ferdinand C.	Duluth
‡	Jacott, William E.	Duluth
‡	Jeronimus, Henry J.	Duluth
‡	Jimenez, Edward	Duluth
‡	Johnson, Franklin L.	Duluth
‡	Johnson, Karl E.	Duluth
‡	Johnson, Randall	Duluth
‡	Johnson, Theodore L.	Duluth
‡	Juntunen, Roy R.	Duluth
‡	Kilen, Mark B.	Duluth
†‡	Klein, Harry	Duluth
‡	Knabe, George W., Jr.	Duluth
‡	Knoedler, John P.	Duluth
	Kosiak, William	St. Paul
‡	Kubista, Theodore P.	Duluth
‡	Kundel, Donald W.	Duluth
‡	Kwako, Jerome E.	Duluth
‡	L'Abbe, A. J. Philip	Duluth
‡	LaBree, Robert H.	Duluth
‡	Larson, Donald M.	Duluth
	Larson, Kenneth R.	Moose Lake
‡	Latterell, Kenneth E.	Duluth
‡	Leek, Joseph H.	Duluth
	Leonardson, Peter Y.	Silver Bay
	Leppo, N. Erkki A.	Duluth
‡	Linnell, Leonard S.	Duluth
†‡	Litman, Samuel N.	Duluth
	Lundberg, Kay R.	Duluth
	Lundberg, Willard	Duluth
†‡	McNutt, John R.	Duluth
	MacDonald, Roger A.	Grand Marais
†	MacRae, Gordon C.	Duluth
†	Martin, Webster C.	Duluth
‡	Maryland, Daniel L.	Duluth
‡	Mathers, John E.	Duluth
‡	Mattson, Roger A.	Duluth
‡	May, Horst G.	Duluth
‡	Mendesh, Anthony N.	Duluth
‡	Merrick, William G.	Duluth
‡	Meyer, Howard J.	Duluth
	Moller, Julie C.	Duluth
‡	Mongé, James J.	Duluth
‡	Monserud, Nels O.	Cloquet
‡	Moyer, John B.	Duluth
	Munger, James E.	Duluth
	Munson, Martin S.	Moose Lake
‡	Myers, Thomas T., III	Duluth
‡	Nisius, George F.	Duluth
‡	Nisswandt, Albert L.	Duluth
†	Norberg, Carl E.	Los Altos, CA
‡	O'Neill, John C.	Duluth
	Olson, Clyde R.	Duluth
£	Ostergaard, Daniel J.	Duluth
‡	Parson, E. Irvine	Duluth
‡	Pasek, Antone W.	Cloquet
	Patch, Orien B.	Duluth
‡	Peterson, John H.	Duluth
	Peterson, Norman P.	Duluth
	Pfeffer, David W.	Duluth
	Pollard, William S.	Duluth
‡	Power, John E.	Duluth
	Puumala, Barbara M.	Cloquet
	Puumala, Reino H.	Cloquet
	Puumala, Ricard R.	Cloquet
‡	Reardon, Andrew E.	Duluth
‡	Reed, Henry H.	Duluth
‡	Rowe, Richard G.	Duluth
‡	Rudie, Peter S.	Duluth
‡	Rudie, William D.	Duluth
‡	Runquist, John M.	Duluth
	Ruth, Bradley R.	Duluth
‡	Ryan, Edward A.	Duluth
	Saloum, Lucille M.	Duluth
	Sanford, John B.	Duluth
	Sax, Milton H.	Duluth
	Schmid, John F.	Duluth
†	Schneider, Lawrence E.	Duluth
‡	Shirley, Raymond M.	Duluth
	Slack, William J.	Duluth
‡	Smith, Cyril M.	Duluth
	Smith, Wallace R.	Grand Marais
†	Spang, Anthony J.	Duluth
†‡	Spang, James S.	Duluth
‡	Spang, William M.	Duluth
‡	Spencer, Joseph F.	Duluth
‡	Stewart, John W.	Duluth
‡	Stolee, Thomas A.	Duluth
‡	Storsteen, Kenneth A.	Duluth
‡	Streitz, John M.	Duluth
‡	Strewler, Gordon J.	Duluth
‡	Swedberg, William A.	Duluth
‡	Swensen, Don P.	Duluth
†	Swenson, Arnold O.	Ft. Myers, FL
	Swenson, Orville P.	Cloquet
	Teich, Kenneth W.	McKeesport, PA
	Terrell, Bernard J.	Nopeming
‡	Tetlie, James P.	Duluth
‡	Thomas, John V.	Duluth
‡	Thompson, James I.	Duluth
‡	Thurn, Roy J.	Duluth
‡	Tosseland, Noel E.	Duluth
‡	Tygart, Robert L.	Duluth
‡	Ulrich, Emery E.	Duluth
	Van Druten, William A.	Duluth
‡	Van Puffelen, Paul S.	Duluth
	Van Ryzin, Donald J.	Duluth
‡	Wahman, Robert E.	Duluth
‡	Walder, Harold J.	Duluth
‡	Wall, Jack E.	Duluth
‡	Wallace, Martin O.	Duluth
†‡	Wells, Arthur H.	Duluth
‡	Williams, Bruce F. P.	Duluth
‡	Wolfe, John W.	Duluth
‡	Young, Hadley R.	Duluth
‡	Young, Joe A.	Duluth

SCOTT-CARVER COUNTY MEDICAL SOCIETY

Scott and Carver Counties
Regular meetings, first Wednesday of March, June,
September and December
Annual meeting in December
Number of members 44

	PRESIDENT	
	Crislip, George D.	Waconia
	SECRETARY	
	Abrams, Donald	Shakopee
	Abrams, Donald J.	Shakopee
	Adams, Patrick J.	Burnsville
	Amra, Waleed	Chaska
	Bean, Charles N.	Waconia
	Berg, John H.	Montgomery
‡	Bratholdt, James W.	Watertown
†	Buck, Frederick H.	Shakopee
	Burkland, Carl E.	New Prague
‡	Cervenka, Charles F.	New Prague
	Cervenka, John D.	New Prague
£	Cowger, Robert C.	Farmington
‡	Crislip, George D.	Waconia
‡	Doherty, Elmer M.	New Prague
	Erickson, Robert L.	Rosemount
‡	Hallgren, Roger	Belle Plaine
	Heagle, C. Russell	Waconia
†	Hebeisen, Milton B.	Chaska
	Heinz, Ivy	Shakopee
‡	Heinzerling, Carl R.	Chaska
	Huang, Ta Yu	Waconia
†‡	Juergens, Herman M.	Belle Plaine
	Kassulke, Jan I.	Shakopee
†	Kucera, Stanley T.	Northfield
‡	Kuz, Eugene	Savage
	Labayen, Ricardo A.	Waconia
	Larson, Leighton W.	Savage
	Lehmann, James D.	Waconia
‡	Lehrer, Alfred J.	Montgomery
‡	Lukk, Olaf	Prior Lake
†	McDaniel, Samuel P.	Lakeville
	Mendiola, Ramon P., Jr.	Waconia
‡	Olson, Richard E.	Chaska
‡	Pearson, Bror F.	Shakopee
‡	Philp, David R.	Watertown
‡	Pistulka, Rolland D.	Chaska
	Ponterio, James E.	Shakopee
	Provence, Cecil L.	Waconia
†‡	Schimelpfenig, George T.	Chaska
‡	Spagnolo, Anthony A.	Shakopee
	Stahler, Paul A.	Jordan
	Wempner, Jon D.	Waconia
†‡	Westerman, Alvin E.	Montgomery
†‡	Westerman, Fred C.	Montgomery
	Wilcox, Michael R.	New Prague

SIBLEY COUNTY MEDICAL SOCIETY

Sibley County
Regular meetings, 3rd Monday of odd number months
Annual meeting in November
Number of members 5

	PRESIDENT	
	Knoche, Harvey A.	Gaylord
	SECRETARY	
	Bergersen, Dean	Arlington
	Bergersen, Dean	Arlington
†	Dysterheft, Adolph	Gaylord
†	Kath, Reinhard H.	Merrifield
	Knoche, Harvey A.	Gaylord
‡	Vener, John M.	Arlington

SOUTHWESTERN MINNESOTA MEDICAL SOCIETY

Cottonwood, Jackson, Murray, Nobles, Pipestone and
Rock Counties
Regular meetings first Monday of each month
except June, July and August
Annual meeting, November
Number of members 50

	PRESIDENT	
	Carlson, Lloyd E.	Windom
	SECRETARY	
	Boone, Ervin S.	Luverne
‡	Bader, Jean L.	Slayton
‡	Basinger, Harold P.	Windom
†‡	Basinger, Homer P.	Windom
‡	Beckering, Roland G.	Edgerton
†‡	Benjamin, Walter G.	Pipestone
‡	Birkemeyer, Eugene J.	Worthington
†‡	Bofenkamp, Ferdinand W.	Luverne
‡	Boone, Ervin S.	Luverne
	Boyd, Frank E.	Pipestone
‡	Carlson, John V.	Westbrook
‡	Carlson, Lloyd E.	Worthington
‡	Christiansen, Harold A.	Jackson
‡	Dawson, Lorin D.	Worthington
‡	Dokken, James H.	Windom
‡	Doman, Victor W.	Lakefield
‡	Eaton, David B.	Worthington
‡	Faul, Bennie C.	Worthington
‡	Fitch, Charles G.	Worthington
‡	Glick, Dallas D.	Mountain Lake
	Hallin, Roger P.	Minnetonka
†‡	Halloran, Walter H.	Jackson
‡†	Harrison, Percy W.	Worthington
‡	Hegstad, Thomas C.	Windom
‡	Heiberg, O. M.	Worthington
‡	Keyes, Robert W.	Pipestone
†‡	Kilbride, Edwin A.	Worthington
‡	Kim, Kyoung	Worthington
‡	Kotval, Russell J.	Pipestone

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Southwestern Minnesota Medical Society *(Continued)*

‡	Laikola, Leslie A.	Adrian
‡	Lohmann, John G.	Pipestone
‡	Lyon, Larry E.	Luverne
‡	Minge, Raymond K.	Worthington
‡	Mork, John N.	Worthington
‡	Nealy, Donald E.	Adrian
‡	Nywall, Dean D.	Slayton
‡	Odland, Donald M.	Luverne
‡	Olson, David E.	Worthington
‡	Patterson, Hugh D.	Slayton
‡	Pierson, Roy F.	Slayton
‡	Plucker, Milton W.	Worthington
‡	Rud, Paul D.	Luverne
	Ryding, Vincent	Fargo, ND
‡	Seisler, Edward P.	Worthington
‡	Siebert, Darrel W.	Luverne
‡	Stam, John	Worthington
‡	Strand, Jack W.	Jasper
‡†	Sratte, Harold C.	Windom
‡	Strough, LaVern C.	Worthington
‡	Wells, Walter B.	Jackson
‡	Wiens, Alvin L.	Mountain Lake

STEARNS-BENTON COUNTY MEDICAL SOCIETY

Stearns and Benton Counties
Regular meeting, Third Thursday of nine months
Annual meeting, second Thursday in December
Number of members 108

PRESIDENT
Murray, Robert .... St. Cloud
SECRETARY
Espelien, Alan D. .... St. Cloud
SECRETARY, EXECUTIVE OFFICE
Bauer, Mrs. Jean .... St. Cloud

‡	Alden, Charles W.	Sauk Rapids
	Aulick, Ernest J.	Paynesville
‡	Autrey, William A.	St. Cloud
	Ballantine, Jerome J.	St. Cloud
‡	Bancroft, Burton R., Jr.	St. Cloud
	Bauman, John C.	Foley
‡	Baumgartner, Florian H.	Albany
	Belshe, Joseph	St. Cloud
‡	Berger, Phil R.	St. Cloud
‡	Beuning, John B.	St. Cloud
‡	Bozanich, Milosh S.	St. Cloud
‡	Brattensborg, Henry J.	St. Cloud
‡	Brigham, Charles F., Jr.	St. Cloud
‡	Broker, Henry M.	St. Cloud
‡	Brown, Frank T.	St. Cloud
‡	Burmaster, Robert W.	St. Cloud
	Cesnik, Robert J.	Sauk Rapids
	Chawla, Ramesh C.	Milaca
	Cress, Thomas L.	St. Cloud
‡	Cumming, Robert J.	St. Cloud
	Dahlquist, LaRue V.	St. Cloud
‡	DeVinck, James F.	St. Cloud
†‡	Donaldson, Charles S.	St. Cloud
	Dubois, Julian F.	Sauk Centre
‡	Dziubinski, Emil H.	St. Cloud
‡	Ehlen, Charles P.	St. Cloud
‡	Espeland, L. Michael	St. Cloud
‡	Espelien, Alan D.	St. Cloud
‡	Evans, Leslie M.	Sauk Rapids
‡	Gaida, Joseph B.	St. Cloud
	Gerstenkorn, George B.	Milaca
‡	Goehrs, Gilman H.	St. Cloud
	Gonzales, Neva M.	St. Cloud
	Grant, John C.	Sauk Centre
†	Halenbeck, Philip L.	St. Cloud
‡	Harbaugh, John T.	St. Cloud
‡	Held, William J.	St. Cloud
†	Henry, Clarence J.	Onamia
	Henry, Joseph E.	Milaca
‡	Hobday, H. Thomas	St. Cloud
	Horn, Allan	Melrose
	Hughes, Bernard J.	St. Cloud
‡	Iverson, Jerry A.	St. Cloud
‡	Jaeger, Dwight E.	St. Cloud
‡	John, Byron L.	St. Cloud
‡	Johnson, William E.	St. Cloud
	Keith, Paul J.	Milaca
‡	Kelly, James H.	St. Cloud
‡	Kelly, John F.	Cold Spring
‡	Koop, Severin H., Jr.	St. Cloud
‡	Kruzich, Stephen J.	St. Cloud
	Kuhlmann, Lawrence B.	Melrose
‡	Kvistberg, Gerald K.	St. Cloud
‡	LaFond, Edward M.	St. Cloud
‡	Lenarz, Albert J.	St. Cloud
	Lindeman, Raymond J.	Paynesville
‡	Loeb, George L.	St. Cloud
‡	Loes, Louis, A.	St. Cloud
‡	Luby, Thomas H.	St. Cloud
‡	Lyons, John R.	St. Cloud
†	McDowell, John P.	St. Cloud
	McNamara, John P.	Rice
‡	May, Robert B.	St. Cloud
†	Milhaupt, Emmett N.	Dunedin, FL
‡	Moran, Paul T.	St. Cloud
	Mueller, Rudolph B.	Richmond
‡	Murn, Thomas G.	St. Cloud
‡	Murray, Robert A., Jr.	St. Cloud
‡	Neils, Vernon E.	St. Cloud
	Nietfield, Aloys B.	Sauk Centre
‡	O'Keefe, James P.	St. Cloud
‡	Olinger, John N.	St. Cloud
‡	Osteraas, Grayson	St. Cloud
	Park, Myung C.	St. Cloud
‡	Petersen, Robert T.	St. Cloud
‡	Phares, Otto C.	St. Cloud
‡	Raetz, Sylvester J.	Maple Lake
‡	Rafferty, Robert F.	St. Cloud
‡	Ranson, H. Robert	St. Cloud
‡	Rice, William H.	St. Cloud
†	Richards, William B.	St. Cloud
‡	Ritchie, Donald A.	St. Cloud
‡	Rovelstad, Roger A.	St. Cloud
‡	Rozycki, Anthony T.	St. Cloud
	Salk, Richard J.	Albany
	Savelkoul, Gene R.	Belgrade
	Scanlan, Timothy N.	Melrose
	Schamber, Walter	St. Cloud
‡	Schlorf, Richard A.	St. Cloud
‡	Schmitz, Everett J.	St. Cloud
	Sisk, Harvey E.	St. Cloud
‡	Slanga, Roger A.	St. Cloud
‡	Smith, J. Weston	St. Cloud

Stearns-Benton County Medical Society *(Continued)*
‡ Sommers, Stephen D. .... St. Cloud
‡ Stahn, Louis H. .... St. Cloud
‡ Stiles, Clifford D. .... Foley
‡ Thienes, R. Lawrence .... St. Cloud
Thuringer, Carl B. .... St. Cloud
‡ Urbanyi, Eugene W. .... St. Cloud
Vanderpool, Thomas E. .... Paynesville
Van Nostrand, David M. .... St. Cloud
‡ Warner, Paul L. .... St. Cloud
‡ Wenner, Waldemar T. .... St. Cloud
‡ Williamson, Kenneth R. .... St. Cloud
Windschitl, Harold E. .... St. Cloud
‡ Wittrock, Louis H. .... St. Cloud
† Zachman, Albert H. .... Melrose
‡ Zeleny, Joseph H. .... St. Cloud

STEELE COUNTY MEDICAL SOCIETY

Steele County
Regular meetings, third Tuesday every other month
Annual meeting, third Tuesday of January
Number of members 23

PRESIDENT
deWerd, Robert .... Owatonna
SECRETARY
Miller, James D. .... Owatonna
‡ Anderson, Franklin C. .... Owatonna
Arnesen, John F. .... Owatonna
‡ Benjamin, Roger J. .... Owatonna
‡ Buresh, Kenneth L. .... Owatonna
‡ deWerd, Robert W. .... Owatonna
Dewey, Donald H. .... Owatonna
Floersch, Adrian J. .... Owatonna
Glass, David E. .... Owatonna
‡ Halvorsen, Daniel K. .... Owatonna
* Hatung, Elmer H. .... Claremont
Henry, John C. .... Owatonna
‡ Henry, Kenneth G. .... Owatonna
‡ Hilker, Robert T. .... Owatonna
Honath, Donald H. .... Owatonna
Kulstad, Oscar S. .... Dodge Center
‡ Lundquist, Curt W. .... Owatonna
McEnaney, James E. .... Owatonna
*†‡McIntyre, John A. .... Owatonna
‡ Miller, James D. .... Blooming Prairie
Nealy, Timothy E. .... Blooming Prairie
‡ Olson, Albert J. .... Owatonna
†‡ Roberts, Oliver W. .... Owatonna
† Schaefer, Joseph F. .... Sun City, AZ
Stransky, Theodore W. .... Owatonna
† Wilkowske, Rudolph J. .... Owatonna

UPPER MISSISSIPPI MEDICAL SOCIETY

Aitkin, Cass, Crow Wing, Hubbard, Morrison, Todd & Wadena Counties
Regular meetings, January, April, September
Annual meeting, January
Number of members 75

PRESIDENT
Marshall, Clark M. .... Crosby
SECRETARY
Anderson, Arden O. .... Brainerd
‡ Aga, John H. .... Brainerd
‡ Anderson, Arden O. .... Brainerd
Belcher, Royden A. .... Little Falls
‡ Bissinger, Lester L. .... Brainerd
† Borgerson, Arthur H. .... Long Prairie
Brown, Russell T. .... Browerville
Cardle, George E. .... Brainerd
Carson, John F. .... Aitkin
Churchill, Jane .... Park Rapids
Closuit, Frederick C. .... Aitkin
‡ Coombs, Carl H. .... Cass Lake
Crow, Earl R. .... Minnetonka
† Davis, Lloyd T. .... Wadena
Davis, Luther F. .... Wadena
‡ Dodson, Albertus F. .... Brainerd
Doty, Joseph .... Little Falls
† Erickson, Alvin O. .... Long Prairie
‡ Fitzsimons, William E. .... Brainerd
Fortier, George M. A. .... Little Falls
Fortier, George M. A., Jr. .... Little Falls
Gamm, Edgar R. .... Park Rapids
† Ghostley, Mary C. .... Bemidji
Grimes, Paul T. .... Park Rapids
† Grose, Frederick N. .... Clarissa
Hansen, Milo L. .... Little Falls
Heid, James K. .... Little Falls
‡ Johnson, Douglas L. .... Brainerd
‡ Kanne, Earl R. .... Brainerd
Kelley, Roger E. .... Crosby
Knipp, William J. .... Brainerd
†‡ Knoll, W. V. .... Brainerd
Kohls, Gary G. .... Milaca
‡ Kussy, James C. .... Little Falls
Larson, Donald R. .... Crosby
Larson, Theodore G. .... Brainerd
*† Lee, Hubert W. .... Brainerd
Lelwica, Thaddeus J. .... Staples
Longfellow, Helen .... Brainerd
*† Lund, Werner J. .... Staples
McIlroy, Gary .... Brainerd
†‡ McLane, William O. .... Brainerd
Marshall, Clark M. .... Crosby
‡ Marvin, Joseph E. .... Brainerd
‡ Meller, Maurice .... Brainerd
Mennis, William I. .... Staples
Mortenson, Howard O. .... Menahga
† Mosby, Maurice E. .... Long Prairie
‡ Muesing, Mark A. .... Brainerd
Muus, John H. .... Staples
Ness Duane E. .... Wadena
Nixon, James B. .... Crosby
Olson, Lillian A. .... Ah-Gwah-Ching

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Upper Mississippi Medical Society *(Continued)*

	Parker, Warren E.	Sebeka
‡	Pedersen, Robert L.	Brainerd
‡	Pelzl, Charles R.	Pine River
†	Petraborg, Harvey T.	Aitkin
	Poppie, Robert W.	Brainerd
‡	Reichelt, Leland G.	Wadena
	Ringle, Otto F.	Walker
	Rose, Robert J.	Park Rapids
	Scanlon, Hugh A.	Little Falls
	Schmitt, Tim B.	Browerville
	Schulberg, Verne A.	Minneapolis
	Seifert, Donald R.	Little Falls
	Smith, Baxer A. Jr.	Crosby
	Soriano, Dominador B.	Onamia
	Spieler, Forrest B.	Pequot Lakes
†‡	Stein, Raymond J.	Pierz
	Stoy, Robert A.	Little Falls
	Thompson, V. James	Staples
‡	Vandersluis, Charles W.	Minneota
‡	Watson, Sidney W.	Little Falls
‡	Weaver, John A.	Brainerd
	Weber, Rick	Staples
‡	Westley, Kent F.	Little Falls
	Wiger, Oliver E.	Little Falls
	Williams, Mervyn M.	Ah-Gwah-Ching

WABASHA COUNTY MEDICAL SOCIETY

Wabasha County
Regular meetings, special call
Annual meeting first Thursday after first Monday in October
Number of members 10

PRESIDENT
Ellis, Earl ....Elgin
SECRETARY
Bowers, R. N. ....Lake City

‡	Bouquet, Bertram J.	Wabasha
‡	Bowers, Robert N.	Lake City
‡	Ellis, Earl W.	Elgin
‡	Feigal, Gary R.	Lake City
‡	Gjerde, William P.	Lake City
†	Habein, Harold C.	Palo Alto, CA
‡	Mahle, Donald G.	Wabasha
	Moline, Doreen Martin	Pepin, WI
‡	Sontag, David W.	Lake City
‡	Timm, Marvin E.	Wabasha

WAKOTA MEDICAL SOCIETY

Washington and Dakota Counties
Regular meetings second Tuesday in each month
Annual meeting, December
Number of members 33

PRESIDENT
Diessner, A. W. ....Stillwater
SECRETARY
Quinn, Paul V. ....Stillwater

‡	Bealka, Neil	Stillwater
	Canine, James L.	So. St. Paul
	Dale, Les N.	Hastings
‡	deLeon, Ben	Stillwater
‡	Diessner, Ardell W.	Stillwater
	Fasbender, Herman T.	Hastings
	Foderick, John W.	Hastings
†	Holcomb, Joel T.	Marine-on-the-St. Croix
	Hunter, Murray H.	Farmington
‡	Jensen, James E.	Stillwater
‡	Johnson, O. Guy	St. Paul
†	Just, Herman J.	Hastings
‡	Kiolbasa, Edward B.	Stillwater
	Knott, John	Forest Lake
‡	McCarten, Francis M.	Stillwater
	Midboe, Gilbert T.	Forest Lake
‡	Murphy, Thomas R.	Stillwater
	Nerothin, Paul	Forest Lake
	Paguyo, Nelson	So. St. Paul
	Peikert, Carl F.	Forest Lake
	Purdie, J. L.	Forest Lake
‡	Quinn, Paul	Stillwater
*	Reid, James W.	So. St. Paul
	Ruggles, George M.	Forest Lake
	Sandkamp, Virgil	So. St. Paul
‡	Schulz, Jerome E.	Stillwater
	Schwartz, Carl	Hastings
	Setness, Peter	Forest Lake
†	Sherman, Carnot H.	Bayport
	Standefer, James	Stillwater
‡	Stratte, Jon R.	Stillwater
†	Van Meier, Henry	Stillwater
	Weiss, Carl A.	Hastings
	Zeller, Hector	Hastings

WASECA COUNTY MEDICAL SOCIETY

Waseca County
Regular meeting, December
Annual meeting, December
Number of members 8

PRESIDENT
Gray, Mark A. ....Waseca
SECRETARY
Dey, James W. ....Waseca

	Davis, Raymond D.	Stockton, CA
‡	Dey, James W.	Waseca
‡	Gray, Mark A.	Waseca
‡	Hergott, Patrick	Waseca
‡	Hottinger, Raymond C.	Janesville
‡	Normann, Stephen T.	Waseca
‡	Oeljen, S. C. G.	Waseca
‡	Olds, George H.	New Richland

WEST CENTRAL MINNESOTA MEDICAL SOCIETY

Big Stone, Pope, Stevens and Traverse Counties
Regular meetings, third Tuesday in March, May,
September and November
Annual meeting, November
Number of members 22

PRESIDENT
Rossberg, R. A. ....Morris
SECRETARY
Popoff, Russel G. ....Graceville
£ Benjamin, Charles I. ....St. Paul
*† Bergan, Otto ....Clinton
†‡ Bucher, Foster D. ....Starbuck
£ Christenson, Carl E. ....New Brighton
Colago, Victor M. ....Browns Valley
Eide, O. A. ....Hancock
Halvorsen, John G. ....Clinton
Hedemark, Homer H. ....Ortonville
*† Hedemark, Truman A. ....Ortonville
Karn, Jacob F. ....Ortonville
Knip, Robert J. ....Ortonville
Kooda, Jennings C. ....Morris
Kozel, William J. ....Morris
Larsen, Fran J. ....Clinton
Lee, Gordon E. ....Glenwood
Merrill, Robert ....Des Moines, IA
‡ Pettko, Josef ....Wheaton
Poole, James ....Wheaton
‡ Popoff, Russel G. ....Graceville
‡ Rossberg, Raymond A. ....Morris
Stock, John F. ....Morris
Swedenburg, Paul ....Glenwood
Watson, Robert M. ....Morris
Zempel, Alan R. ....Starbuck

WINONA COUNTY MEDICAL SOCIETY

Winona County
Regular meetings, second Tuesday in January, April,
July and October
Annual meeting, January
Number of members 39

PRESIDENT
Andersen, Horace ....Winona
SECRETARY
Heise, Herbert vR. ....Winona
‡ Andersen, Horace J. ....Winona
Bunnell, Harris F. ....Winona
‡ Casperson, Tom ....Winona
†‡ Christensen, Eli E. ....Winona
‡ DeGallier, Daniel ....Winona
‡ Edin, Andrew E. ....Winona
‡ Fenske, Arnold ....Winona
Finkelnburg, William O. ....Winona
‡ Garber, George L. ....Winona
‡ Haesly, Warren W. ....Winona
‡ Hartwich, Roger F. ....Winona
Hawk, Dale J. ....St. Charles
Heise, Carl vR. ....Winona
‡ Heise, Herbert vR. ....Winona
‡ Heise, Paul vR. ....Winona
Heise, William vR. ....Winona
‡ Herland, Alexander L. ....Winona
‡ Hughes, Sidney O. ....Winona
‡ Johnson, Curtis M. ....Winona
‡ Johnston, Leonard ....Winona
‡ Loomis, George L. ....Winona
† Meinert, Albert E. ....Winona
Miller, Linda K. ....Rochester
‡ Mulrooney, John G. ....Winona
‡ Peterson, John R. ....Rushford
‡ Roemer, Henry J. ....Winona
‡ Rogers, Charles W. ....Winona
‡ Schafer, Charles F. ....Winona
† Schmidt, Hilmar R. ....Winona
Stewart, Richard O. ....Winona
‡ Testor, James V. ....Winona
‡ Tweedy, John A. ....Winona
‡ Tweedy, Robert B. ....Winona
‡ Vieiralves, G. M. ....Winona
‡ Weiss, Joseph E. ....Winona
‡ Wilmot, Thomas M. ....Winona
Wilson, L. J. ....Rushford
† Wilson, R. H. ....Winona
†‡ Younger, Lewis I. ....Winona

WRIGHT COUNTY MEDICAL SOCIETY

Wright County
Regular meetings, first Tuesday of every other month
Annual meeting in November
Number of members 18

PRESIDENT
Sandeen, Robert M. ....Buffalo
SECRETARY
Shin, Rok ....Howard Lake
‡ Anderson, Waldo P. ....Buffalo
†‡ Bendix, Lester H. ....Annandale
Bentzen, C. K. ....Monticello
‡ Cady, Timothy J. ....Buffalo
‡ Catlin, Theodore J. ....Buffalo
Greenfield, Theodore ....Champlin
‡ Guilfoile, Pierre J. ....Delano
†‡ Hart, William E. ....Monticello
Maus, Donald J. ....Monticello
‡ Ourada, Anthony L. ....Maple Lake
Purves, G. Harland ....Buffalo
‡ Sandeen, Robert M. ....Buffalo
‡ Shin, Rok ....Howard Lake
‡ Smorstok, Matthew B. ....Monticello
Steiner, Andrew M. ....St. Michael
†‡ Thielen, R. D. ....New Brighton
‡ Whitesell, L. A., Jr. ....Buffalo
‡ Zapf, John D. ....Monticello

ZUMBRO VALLEY MEDICAL SOCIETY

Olmsted, Houston, Fillmore and Dodge Counties
Regular meetings, first Wednesday of every
odd-numbered month
Annual meeting, November
Number of members 514

PRESIDENT

	Burke, Edmund C.	Rochester

SECRETARY

	Sauer, Robert L.	Preston

EXECUTIVE SECRETARY

	Stickney, J. M.	Rochester
‡	Aaro, Leonard A.	Rochester
£	Abbound, Charles F.	Oronoco
‡	Adson, Martin A.	Rochester
	Affeldt, Daniel E.	Kasson
†	Ahlfs, Jacob J.	Ft. Lauderdale, FL
‡	Ahmann, David L.	Rochester
‡	Allen, George L.	Rochester
£	Alper, Richard E.	Minneapolis
‡	Andersen, Howard A.	Rochester
‡	Anderson, Carl F.	Rochester
†	Anderson, Mark J.	Sun City, AZ
‡	Anderson, Markham J., Jr.	Rochester
#	Anderson, Michael D.	FPO, San Francisco, CA
‡	Anderson, Milton W.	Rochester
#	Applestein, Bruce	Chicopee, MA
£	Ascough, Bruce M.	Panorama City, CA
£	Atwell, David T.	Rochester
£	Bachand, Romeo T., Jr.	Rochester
‡	Baggenstoss, Archie H.	Rochester
£	Bailly, Richard C.	Camp Lejeune, NC
†	Bair, Hugo L.	Rochester
	Baird, Raymond L.	Reno, NV
¶	Bajec, Dusan	Poljame, Yugoslavia
†‡	Baker, George S.	Rochester
‡	Baker, Hillier L., Jr.	Rochester
	Balfour, William M.	Lawrence, KS
‡	Banfield, Frederick D.	Rochester
‡	Banner, Edward A.	Rochester
£	Bardsley, William T. Y.	Rochester
£	Barrett, David M.	Rochester
£	Barron, Stephen B.	Rochester
‡	Barry, Maurice J., Jr.	Rochester
‡	Bartholomew, Lloyd G.	Rochester
‡	Bastron, James A.	Rochester
‡	Bayrd, Edwin D.	Rochester
‡	Beabout, John W.	Rochester
‡	Beahrs, Oliver H.	Rochester
‡	Beck, James P.	Rochester
#	Beckenbaugh, Robert D.	Ft. Hood, TX
£	Beckerman, Stephen B.	Rochester
#	Beckley, James M.	Ft. Hood, TX
‡	Belau, Paul G.	Rochester
‡	Bennett, Clayton J.	Rochester
‡	Berge, Kenneth G.	Rochester
†‡	Berkman, John M.	Rochester
£	Bert, Jeffrey K.	Rochester
‡	Bianco, Anthony J., Jr.	Rochester
‡	Bickel, William H.	Rochester
‡	Bisel, Harry F.	Rochester
‡	Black, B. Marden	Rochester
‡	Black, Leo F.	Rochester
£	Black, Steven B.	Rochester
	Bohrer, James A.	Austin
#	Boren, Gregory G.	Ft. Hood, TX
†‡	Boyd, David A., Jr.	Rochester
†	Braasch, William F.	Rochester
‡	Brandenburg, Robert O.	Rochester
£	Braun, Donald P.	Rochester
£	Breadon, George E.	Rochester
#	Breivis, James S.	Spokane, WA
#	Brewster, Robert C.	Grand Forks, ND
£	Brinton, Edward H.	Rochester
‡	Brodhun, John C.	Rochester
†	Brown, Alex E.	Bradenton, FL
‡	Brown, Arnold L.	Rochester
‡	Brown, Henry A.	Rochester
‡	Brown, Joe R.	Rochester
	Brown, Larry R.	Rochester
†‡	Brown, Philip W.	Rochester
‡	Brubaker, Richard F.	Rochester
¶	Buchholz, Roger M. (Mr.)	St. Cloud
†	Buie, Louis A.	Rochester
‡	Burgert, E. O., Jr.	Rochester
£	Burgher, Louis W.	Rochester
‡	Burich, Harry F.	Rochester
‡	Burke, Edmund C.	Rochester
#	Bush, David J.	Biloxi, MS
‡	Butt, Hugh R.	Rochester
£	Buzanowski, Krystyna	Rochester
‡	Cain, James C.	Rochester
‡	Callahan, John A.	Rochester
‡	Cameron, Alan J.	Rochester
‡	Campbell, Donald C.	Rochester
‡	Campbell, Malcolm K.	Rochester
£	Cannon, Patrick J.	Rochester
‡	Carlson, Harley C.	Rochester
£	Carlson, Richard A.	Rochester
	Carney, Francoise	Rochester
	Carney, John A.	Rochester
	Carr, David T.	Rochester
‡	Carryer, Haddon M.	Rochester
‡	Carter, Earl T.	Rochester
£	Carter, M. Gary	Rochester
£	Chesebro, James H.	Rochester
£	Chiavetta, Stephen V., Jr.	Rochester
‡	Childs, Donald S., Jr.	Rochester
‡	Christensen, Norman A.	Rochester
‡	Christiana, Richard L.	Rochester
†	Clark, Edward C.	San Francisco, CA
£	Clark, Paul S.	Rochester
‡	Cody, D. Thane	Rochester
£	Cody, Michael C.	Rochester
‡	Colby, Malcolm Y., Jr.	Rochester
#	Coleman, Robert L.	Shawnee Mission, KS
£	Conn, Richard L.	Rochester
‡	Cooper, Talbert	Rochester
#	Cooperman, Avram M.	Cleveland, OH
†	Corbin, Kendall B.	Sarasota, FL
‡	Corrigan, Cyril J.	Rochester
£	Cortese, Denis A.	Rochester
‡	Coventry, Markham B.	Rochester
£	Crowder, David F.	Rochester
£	Csir, Floyd M.	Rochester
‡	Culp, Clyde E.	Rochester
§	Culp, Kim S.	Minneapolis
‡	Culp, Ormond S.	Rochester
	Cupps, Roger E.	Rochester
‡	Dahlin, David C.	Rochester
‡	Dale, Allan J. D.	Rochester
‡	Daugherty, Guy W.	Rochester
£	Dauphine, Richard T.	Rochester
†	Davis, Austin C.	Pompano Beach, FL

Zumbro Valley Medical Society *(Continued)*

‡	Davis, George D.	Rochester
£	Davis, Zev	Rochester
‡	Dearing, William H.	Rochester
¶	DeBus, Robert L. (Mr.)	Rochester
‡	Decker, David G.	Rochester
£	DeCourcy, Donald M., Jr.	Rochester
	Deering, Timothy B.	Rochester
£	Derbenwick, Kenneth P.	Rochester
£	Derbenwick, Mary J.	Rochester
‡	DeRemee, Richard A.	Rochester
‡	DeSanto, Lawrence W.	Rochester
‡	Devine, Kenneth D.	Rochester
	Devloo, Robert A.	Rochester
‡	DeWeerd, James H.	Rochester
£	Diaz-Buxo, Jose A.	Rochester
‡	Didier, Edward P.	Rochester
‡	Diessner, Grant R.	Rochester
‡	Dinapoli, Robert P.	Rochester
	Dines, David E.	Rochester
¶	Dobbins, Ronald V. (Mr.)	Rochester
‡	Dobyns, James H.	Rochester
‡	Dockerty, Malcolm B.	Rochester
£‡	Donoghue, Francis E.	Rochester
‡	Douglas, Bruce E.	Rochester
£	Douglas, Donald D.	Rochester
‡	Doyle, James R.	Rochester
£	Dozois, Roger R.	Edinburgh, Scotland
†	Drips, Della G.	Rochester
‡	Duane. Drake D.	Rochester
£	DuBoff, Stuart M.	Rochester
	Duncan, Glen M.	Rochester
‡	Dyck, Peter J.	Rochester
‡	Dyer, John A.	Rochester
£	Dyke, David R.	Rochester
‡	Edmondson, John H.	Rochester
†‡	Elkins, Earl C.	Rochester
†	Emmet, John L.	Portland, OR
	Emmons, Patricia R.	Vancouver, Canada
‡	Emslander, Richard F.	Rochester
†	Engels, Edward P.	Lexington, KY
‡	Erich, John B.	Rochester
‡	Erickson, Donald J.	Rochester
‡	Espinosa, Raul	Rochester
#	Ettinger, David S.	Cockneysville, MD
†‡	Faber, John E.	Rochester
‡	Facer, George W.	Rochester
£	Falcone, James C.	Rochester
†‡	Faulconer, Albert, Jr.	Rochester
	Feldmann, Floyd M.	Pompano Beach, FL
‡	Ferguson, Richard H.	Rochester
†‡	Ferris, Edward O.	Rochester
£	Field, Charles S.	Rochester
‡	Fish, Charles R.	Rochester
£	Folger, Walter N.	Rochester
‡	Fontana, Robert S.	Rochester
†	Foss, Edward L.	Condon, MT
£	Fraser, Richard A.	Rochester
‡	Frethem, Allen A.	Rochester
†	Fricke, Robert E.	Rochester
£	Friedell, Peter E.	Rochester
£	Frytak, Stephen	Rochester
‡	Furlow, William L.	Rochester
£	Fuster, Valentin	Rochester
£	Gall, Randall J.	Rochester
†‡	Gambill, Carl M.	Rochester
†‡	Gambill, Earl E.	Rochester
‡	Garber, James J.	Rochester
£	Gard, Joseph R.	Rochester
‡	Gastineau, Clifford F.	Rochester
‡	Geraci, Joseph E.	Rochester
‡	Gisvold, John J.	Rochester
£	Glista, Glen G.	Rochester
£	Goellner, John R.	FPO, San Francisco, CA
‡	Goldstein, Norman P.	Rochester
‡	Goldston, Edgar C.	Rochester
£	Goldyne, Marc E.	Rochester
‡	Good, C. Allen, Jr.	Rochester
‡	Gorman, Columba A.	Rochester
‡	Gould, Allan B., Jr.	Rochester
#	Gould, Ronauld J.	Rochester
‡	Grabow, Jack D.	Rochester
‡	Graf, John A.	Rochester
£	Grannis, Frederic W. Jr.	Rochester
‡	Gravett, Desmond C.	Rochester
‡	Green, Paul A.	Rochester
‡	Greene, Laurence F.	Rochester
£	Greipp, Philip R.	Rochester
	Greydanus, Donald E.	Hawthorne, NJ
‡	Groover, Robert V.	Rochester
‡	Gross, John B.	Rochester
	Grubbs, Larry T.	Columbus, OH
	Gyory, Attila W.	Rochester
‡	Hagedorn, Albert B.	Rochester
‡	Hahn, Richard G.	Rochester
†‡	Haines, Samuel F.	Rochester
†	Hallberg, Olav E.	Rochester
	Halpin, John A.	Rochester
£	Hancock, William E.	Pomona, CA
‡	Hanlon, David G.	Rochester
£	Hanson, Ernest J., Jr.	Rochester
‡	Hanson, Norbert O.	Rochester
	Hanson, Norman P.	Rochester
†‡	Hargraves, Malcolm M.	Rochester
‡	Hartfield, James E., Jr.	Rochester
‡	Hartman, Glen W.	Rochester
¶	Hartmann, Ronald J. (Mr.)	Rochester
£	Hartzler, Geoffrey O.	Rochester
¶	Hauff, Karen J. (Ms.)	Rochester
£	Havig, Terrance A.	Lexington, KY
#	Hayashi, Melvin M. K. W.	Belleville, IL
‡	Hayles, Alvin B.	Rochester
†	Heck, Frank J.	Rochester
¶	Heidel, Werner	Cresskill, NJ
£	Heiss, Frederick W.	Rochester
†	Helgason, Pall B.	Rochester
£	Heller, Stephen F.	Rochester
‡	Helmholz, Henry F., Jr.	Rochester
‡	Henderson, Edward D.	Rochester
‡	Henderson, John W.	Rochester
‡	Henderson, Lowell L.	Rochester
£	Henrickson, Ronald R.	Rochester
‡	Hepper, Norman G.	Rochester
‡	Hermans, Paul E.	Rochester
	Herrell, Wallace E.	Rochester
†	Hewitt, Edith S.	Rochester
‡	Hill, John R.	Rochester
‡	Hill, Richard W.	Rochester
	Hines, Edgar A., Jr.	Black Mountain, NC
£	Hirsche, Blayne L.	Rochester
‡	Hoagland, H. Clark	Rochester
¶	Hodgin, Carol L. (Ms.)	Fargo, ND
†	Hodgson, Corrin J.	Rochester
‡	Hodgson, John R.	Rochester
	Hoffman, David L.	Rochester
	Holbrook, Margaret A.	Rochester
£	Holcomb, Gerald R.	Rochester

(Continued on next page)

Zumbro Valley Medical Society *(Continued)*

	Holland, C. R.	Rochester
‡	Hollenhorst, Robert W.	Rochester
‡	Holman, Colin B.	Rochester
†‡	Horton, Bayard T.	Rochester
‡	Houser, Otis W.	Rochester
‡	Howard, Frank M., Jr.	Rochester
‡	Howell, Llewelyn P.	Rochester
£	Huerta, Enrique	Rochester
‡	Hunder, Gene G.	Rochester
†	Hunt, Arthur B.	Carmel, CA
‡	Hunt, James C.	Rochester
¶	Hunt, Max L., Jr.	Rochester
#	Huston, Kent A.	Wichita, KS
#	Hynes, Kieran M.	Wright-Patterson AFB, OH
‡	Ivins, John C.	Rochester
£	Jackman, Steven J.	Rochester
†‡	Janes, Joseph M.	Rochester
£	Jibilian, Artin Y.	Rochester
‡	Johnson, Carl E.	Rochester
‡	Johnson, Einer W., Jr.	Rochester
£	Johnson, Marvin W.	Rochester
‡	Johnson, William J.	Rochester
£	Jones, Ian V.	Rochester
‡	Jordon, Robert E.	Rochester
‡	Jorgensen, Edward O.	Rochester
‡	Joyce, John W.	Rochester
‡	Judd, Edward S.	Rochester
‡	Kaese, Werner E.	Rochester
#	Kaine, Richard F.	St. Albans, NY
£	Kantack, Paul W.	Kessler AFB, MS
£	Karlowski, Thomas R.	Rochester
‡	Karnes, William E.	Rochester
£	Karrow, John W.	Rochester
‡	Kazmier, Francis J.	Rochester
‡	Kearns, Thomas P.	Rochester
†‡	Keith, Haddow M.	Rochester
†	Keith, Norman M.	Rochester
‡	Kelalis, Panayotis P.	Rochester
‡	Kelly, Patrick J.	Rochester
£	Kelman, Donald B.	Rochester
‡	Kennedy, Charles C.	Rochester
	Kennel, Arthur J.	Rochester
†‡	Kernohan, James W.	Rochester
‡	Kerr, Frederick W. L.	Rochester
£	Key, Samuel N., III	San Francisco, CA
‡	Keys, Thomas F.	Rochester
‡	Kiely, Joseph M.	Rochester
	Kierland, Robert R.	Rochester
	Kim, Hyan-Hahke	San Antonio, TX
	Kimmel, George E.	Evansville, IN
	Kincaid, Owings W.	Rochester
‡	Kirby, Thomas J., Jr.	Rochester
	Kirklin, John W.	Birmingham, AL
	Klass, Donald W.	Rochester
‡	Knutson, Lewis A.	Spring Grove
‡	Konicek, Robert G.	Rochester
¶	Korz, Louise S. (Ms.)	Rochester
¶	Kostick, Joseph (Mr.)	Rochester
£	Krohn, John R.	Rochester
£	Krueger, Bruce R.	Rochester
	Krupp, Neal E.	Rochester
#	Kuge, Mark T.	APO, San Francisco, CA
	Kvamme, Brynjulv	Mabel
‡	Kyle, Robert A.	Rochester
£	Labrecque, Pierre-Georges	Rochester
‡	Lake, Clifford F.	Rochester
£‡	Laws, Edward R., Jr.	Rochester
‡	Leary, Frank J.	Rochester
‡	Lee, Raymond A.	Rochester
‡	Lee, Robert E.	Rochester
£	Leist, Frederick D.	Rochester
‡	Leonard, Paul F.	Rochester
#	Levy, Jonathan M.	Albuquerque, NM
‡	Lillie, John C.	Rochester
‡	Lindsay, Malcolm I., Jr.	Rochester
#	Lippman, Harry H.	San Diego, CA
‡	Litzow, Thaddeus J.	Rochester
‡	Lofgren, Eric P.	Rochester
‡	Lofgren, Karl A.	Rochester
‡	Logan, George B.	Rochester
†‡	Love, J. Grafton	Rochester
¶	Lucas, Charles T.	Rochester
‡	Ludes, Bernard F.	Rochester
£	Luthra, Harvinder S.	Rochester
‡	Lynn, Hugh B.	Rochester
	McBeau, J. B.	Rochester
‡	McConahey, William M., Jr.	Rochester
£	McConahey, William M., III	Rochester
£	McCormack, Lawrence R.	Rochester
‡	McDonald, Thomas J.	Rochester
#	McDuffie, Richard W., Jr.	Ft. Sill, OK
#	McElfresh, Edward C.	Ft. Eustis, VA
#	McGee, Hugh E., Jr.	Ft. Lee, VA
	McGill, Douglas B.	Rochester
	McPhee, Malcolm C.	Rochester
‡	McIlrath, Donald C.	Rochester
‡	McKenna, Charles H.	Rochester
¶	McShane, M. Quentine (Sister)	Rochester
‡	MacCarty, Collin S.	Rochester
£	MacCarty, William C., III	Rochester
	MacDonald, Charles J.	St. Paul
£	MacKenzie, Ronald A.	Rochester
†	MacLean, Alexander R.	Rochester
‡	Madsen, Eugene F.	Rochester
†‡	Magath, Thomas B.	Rochester
	Magid, Gail A.	Santa Cruz, CA
‡	Maher, Frank T.	Rochester
	Malek, Reza S.	Rochester
‡	Malkasian, George D.	Rochester
‡	Mankin, Harold T.	Rochester
£	Marciniak, Thomas A.	Rochester
‡	Marcoux, J. Paul	Rochester
£	Marcus, Walter M.	Rochester
£	Marik, Francis	Rochester
£	Marmer, Robert H.	Rochester
‡	Martens, Theodore G.	Rochester
£	Martimbeau, Pierre	Rochester
‡	Martin, Gordon M.	Rochester
‡	Martin, Harold R.	Byron
¶	Martin, James E. (Mr.)	Rochester
‡	Martin, Maurice J.	Rochester
£	Maruta, Toshihiko	Rochester
£	Mason, Bruce D.	Rochester
†‡	Masson, James C.	Rochester
‡	Masson, James K.	Rochester
†‡	Mathieson, Don R.	Rochester
£	Matlak, Michael E.	Rochester
	Matson, Roland W.	Spring Valley
	Mayberry, William E.	Rochester
	Mayne, John G.	Rochester
‡	Merritt, Wallace A.	Rochester
‡	Messick, Joseph M., Jr.	Rochester
	Miller, John H.	Rochester
‡	Miller, Roland Drew	Rochester
£	Miles, Wayne B.	Rochester
‡	Miller, Ross H.	Rochester
‡	Miller, W. Eugene	Rochester

Zumbro Valley Medical Society *(Continued)*

‡ Millikan, Clark H. ....Rochester
‡ Mills, Stephen D. ....Rochester
# Mitchell, John C., III ....Travis, AFB, CA
† Moersch, Fred P. ....Ft. Lauderdale, FL
Moersch, Herman ....Rochester
£ Mokri, Bahram ....Rochester
‡ Molnar, George D. ....Rochester
† Montgomery, Hamilton ....Rochester
£ Moore, Burton A. ....Rochester
‡ Moore, Gordon L., II ....Rochester
Mori, Hideo ....Grand Meadow
Morimoto, Allen M. ....APO, San Francisco, CA
‡ Morlock, Carl G. ....Rochester
£ Morrey, Bernard F. ....Rochester
‡ Morrow, George W., Jr. ....Rochester
‡ Morse, Robert M. ....Rochester
Muenter, Manfred D. ....Rochester
‡ Mulder, Donald W. ....Rochester
‡ Muller, Sigfrid A. ....Rochester
£ Munoz, Juan M. ....Rochester
† Mussey, Mary E. ....Rochester
Myers, Thomas T. ....Rochester
£ Neel, H. Bryan III ....Rochester
‡ Neault, Roger W. ....Rochester
Nelson, Audrey M. ....Rochester
Nelson, Ralph A. ....Rochester
‡ Nesset, David G. ....Rochester
£ Neupert, Jerrol R. ....Rochester
‡ Newcomer, Albert D. ....Rochester
Nichols, Victoria R. ....Rochester
£ Niven, Robert G. ....Rochester
‡ Nichols, Donald R. ....Rochester
£ Nijensohn, Daniel R. ....Rochester
‡ Nobrega, Fred T. ....Rochester
£ Nolan, Declan R. ....Rochester
‡ Obetz, Samuel W. ....Rochester
£ O'Dea, Michael J. ....Rochester
£ Olivet, Ronald T. ....Rochester
‡ Olsen, Arthur M. ....Rochester
Olson, Grant E. ....West Concord
Olson, John D. ....Rochester
‡ Olson, Neal R. ....Rochester
‡ Onofrio, Burton M. ....Rochester
† Onsgard, L. Kenneth ....St. Petersburg, FL
‡ Opitz, Joachim L. ....Rochester
‡ Osmundson, Philip J. ....Rochester
‡ Owen, Charles A., Jr. ....Rochester
# Oxman, Herbert A. ....San Antonio, TX
‡ Palumbo, Pasquale J. ....Rochester
‡ Parker, Robert L. ....Rochester
† Parkhill, Edith M. ....Rochester
# Parry, Rodney R. ....Ft. Campbell, KY
¶ Patterson, Linda G. ....Rochester
‡ Payne, William S. ....Rochester
† Pease, Gertrude L. ....Rochester
‡ Perry, Harold ....Rochester
‡ Perry, Lawrence B. ....Rochester
† Perry, Michael C. ....Rochester
‡ Peters, Gustavus A. ....Rochester
£ Petersen, Eugene G. ....Rochester
† Petersen, Magnus C. ....Rochester
‡ Peterson, Hamlet A. ....Rochester
‡ Peterson, Lowell F. A. ....Rochester
‡ Petitt, Robert M. ....Rochester
Pettersen, George R. ....Rochester
‡ Peyla, Thomas L. ....Rochester
£ Pfeiffer, Craig N. ....Rochester
‡ Pierre, Robert V. ....Rochester
# Pikler, George M. ....Ft. Polk, LA
‡ Pluth, James R. ....Rochester
£ Plutnicki, Ronald S. ....Rochester
‡ Polley, Howard F. ....Rochester
†‡ Pool, Thomas Lloyd ....Rochester
£ Port, Friedrich K. ....Rochester
‡ Poston, Lawrence M. ....Caledonia
Pougiales, Mary L. P. ....Rochester
£ Prakash, Udaya B. S. ....Rochester
‡ Pratt, Joseph H., Jr. ....Rochester
‡ Prentice, James A. ....Rochester
† Prickman, Louis E. ....Rochester
†‡ Priestly, James T. ....Rochester
‡ Pruitt, Raymond D. ....Rochester
† Pugh, David G. ....Sun City, AZ
‡ Purnell, Don C. ....Rochester
£ Rahimi, Abbas ....Rochester
Raimundo, Hugo Sa ....Rochester
‡ Ralston, Donald E. ....Rocheser
‡ Randall, Raymond V. ....Rochester
£ Rasmussen, Richard W. ....Rochester
Reick, Robert R. ....Independence, IA
‡ Reitemeier, Richard J. ....Rochester
‡ ReMine, William H., Jr. ....Rochester
‡ Restall, Charles J. ....Rochester
Rife, Charles C. ....Rochester
Riley, Fenwick C. ....Rochester
£ Rivers, Thomas A. ....Rochester
Risser, Alden F. ....Stewartville
‡ Ritter, Donald G. ....Rochester
‡ Rivan, Robert J. ....Rochester
‡ Robertson, Dennis M. ....Rochester
£ Robertson, Robert C. ....Rochester
£ Robinson, Gerald N. ....Rochester
Rodarte, Joe R. ....Rochester
£ Rogers, John R. ....Rochester
Rogers, Roy S., III ....Rochester
† Rogne, W. G. ....Spring Grove
‡ Rome, Howard P. ....Rochester
£ Rome, Jeffrey D. ....Rochester
‡ Rooke, E. Douglas ....Rochester
Rosenbaum, Alan H. ....Rochester
‡ Rosenow, Edward C., III ....Rochester
‡ Ross, James V., Jr. ....Rochester
‡ Rovelstad, Randolph A. ....Rochester
Roy, Paul H. J. ....Quebec, Canada
†‡ Rucker, Charles W. ....Rochester
‡ Rushton, Joseph G. ....Rochester
£ Ryan, Dennis K. ....Rochester
†‡ Rynearson, Edward H. ....Rochester
‡ Salassa, Robert M. ....Rochester
‡ Sander, Frank V., Jr. ....Rochester
‡ Sanderson, David R. ....Rochester
‡ Sandok, Burton A. ....Rochester
£ Sanfelippo, Peter M. ....San Antonio, TX
£ Satava, Richard M. ....Rochester
Sauer, Robert L. ....Preston
‡ Sauer, William G. ....Rochester
‡ Sawtell, Robert R. ....Rochester
‡ Scanlon, Paul W. ....Rochester
£ Schafermeyer, Robert W. ....Rochester
‡ Schirger, Alexander ....Rochester
£ Schmerler, Michael ....Rochester
Schneider, Dally L. ....Rochester
Schoenberg, Bruce S. ....Rochester
‡ Scholz, Donald A. ....Rochester
‡ Schroeter, Arnold L. ....Rochester

(Continued on next page)

Zumbro Valley Medical Society *(Continued)*

	Schutt, Allan J.	Rochester
	Schutt, Ann H.	Rochester
¶	Schwartau, Neal W. (Mr.)	Rochester
¶	Schwerman, Earl A., Jr.	Rochester
£	Sciallis, Gabriel F.	Rochester
¶	Scott, James J. (Mr.)	Rochester
#	Sebrechts, Paul	San Diego, CA
	Segura, Joseph W.	Rochester
†‡	Seldon, T. Harry	Rochester
#	Serafano, Donald N.	Davis AFB, AZ
‡	Sessler, Alan D.	Rochester
	Shea, John A.	Rochester
£	Sheehan, Joseph C. M.	Rochester
‡	Sheps, Sheldon G.	Rochester
‡	Shick, Richard M.	Rochester
£	Sidell, Peter M.	Rochester
	Siegmann, William C.	Minneapolis
‡	Siekert, Robert G.	Rochester
‡	Silverstein, Murray N.	Rochester
†‡	Slocumb, Charles H.	Rochester
£	Smigiel, Mitchell R., Jr.	Rochester
‡	Smith, Lucian A.	Rochester
‡	Smith, Ralph E.	Rochester
	Snyder, Robert E.	Spring Valley
‡	Soule, Edward H.	Rochester
‡	Spencer, Robert J.	Rochester
‡	Spiekerman, Ralph E.	Rochester
‡	Spittell, John A., Jr.	Rochester
†‡	Sprague, Randall G.	Rochester
£	Sridaromont, Somkid	Rochester
†‡	Stauffer, Maurice H.	Rochester
‡	Steinhilber, Richard M.	Rochester
	Stephens, David H.	Rochester
£	Stevenson, Edward W.	Rochester
‡	Stickler, Gunnar B.	Rochester
‡	Stickney, J. M.	Rochester
‡	Stillwell, G. Keith	Rochester
†‡	Stilwell, George G.	Rochester
£	Stone, Stephen P.	Rochester
‡	Stonnington, Henry H.	Rochester
†‡	Stroebel, Charles F., Jr.	Rochester
‡	Strong, Cameron G.	Rochester
‡	Stubbs, Samuel E.	Rochester
£	Suh, Ku Won	Rochester
‡	Summerskill, William H.	Rochester
‡	Sundt, Thoralf M., Jr.	Rochester
£	Sung, David T. W.	Rochester
‡	Swanson, David W.	Rochester
£	Swanson, Gene E.	Rochester
#	Swint, Robert E.	29 Palms, CA
#	Tangedahl, Tim N.	Bismarck, ND
‡	Taswell, Howard F.	Rochester
	Thomas, Juergen E.	Rochester
¶	Thompson, Conrad O. (Mr.)	Rochester
†	Thompson, Gershom J.	Rochester
£	Throckmorton, Tom D.	Rochester
‡	Thurber, Deloran L.	Rochester
†‡	Tillisch, Jan H.	Rochester
‡	Tinkham, Robert G.	Rochester
£	Tinstman, Thomas C.	Rochester
‡	Tompkins, Richard B.	Rochester
£	Totz, Robert S.	Rochester
#	Townsend, Gary L.	Abilene, TX
‡	Trautmann, James C.	Rochester
#	Tschetter, Loren K.	Ft. Leavenworth, KS
‡	Tyce, Francis	Rochester
†	Uihlein, Alfred	Rochester
‡	Underdahl, Laurentius O.	Rochester
‡	Utz, David C.	Rochester
¶	Van Groll, Kathleen (Sister)	Rochester
	van Heerden, Jonathan A.	Rochester
	Van Herik, Martin	Rochester
‡	Vaughn, Louis D.	Rochester
£	Verheyden, Charles N.	Rochester
	Virnig, Hildegard J.	Caledonia
	Wahner, Heinz W.	Rochester
¶	Wakim, Khalil G.	Terre Haute, IN
‡	Wallace, Robert B.	Rochester
£	Walser, Adolf H.	Rochester
†‡	Walters, Waltman	Rochester
‡	Ward, L. Emmerson	Rochester
£	Warner, Thomas F. C. S.	Rochester
†	Watkins, Charles H.	Sun City, AZ
#	Webel, Max L.	Silver Spring, MD
‡	Weed, Lyle A.	Rochester
‡	Weeks, Richard E.	Rochester
†‡	Weir, James F.	Rochester
‡	Welch, John S.	Rochester
‡	Wellman, William E.	Rochester
	Wellner, Theodore O.	Rochester
‡	Wente, Harold A.	Rochester
	Westmoreland, Barbara	Rochester
	Westrup, John E.	Lanesboro
‡	Wharton, William P.	Rochester
‡	Whisnant, Jack P.	Rochester
‡	White, Roger D.	Rochester
‡	White, William L.	Rochester
	Wilder, Thomas C. Jr.	Rochester
‡	Wilkowske, Conrad J.	Rochester
	Williams, Sidney D., Jr.	Rochester
‡	Williams, Thomas H.	Rochester
#	Williams, W. Byron	Charleston, SC
£	Willis, Larry F.	Rochester
‡	Wilson, David M.	Rochester
	Wilson, M. Robert, Jr.	Faribault
†‡	Wilson, Robert B.	Rochester
	Wilson, Viktor O.	Rochester
‡	Wiltsie, John C.	Rochester
‡	Winklemann, Richard K.	Rochester
£	Wolf, Stephen A.	Rochester
‡	Wollaeger, Eric E.	Rochester
‡	Wood, Lloyd T.	Rochester
‡	Woods, John E.	Rochester
‡	Woolner, Lewis B.	Rochester
‡	Worthington, John W., Jr.	Rochester
	Yoss, Robert E.	Rochester
†‡	Young, H. Herman	Rochester
£	Zimmerman, Bruce R.	Rochester
£	Zuika, Maris	Rochester

ALPHABETIC ROSTER

Key to Symbols

* Deceased
† Associate and Life
£ Resident and Intern
§ Medical Student
# Service
¶ Affiliate and Honorary

A

	Aadelan, Richard J.	Minneapolis
	Aamath, Gordon M.	Minneapolis
	Aaro, Leonard A.	Rochester
	Aas, Johannes	Duluth
	Aas, Martha A.	Duluth
£	Abboud, Charles F.	Oronoco
	Abraham, Arden L.	Duluth
	Abrams, Alexander, Jr.	St. Paul
	Abrams, Donald J.	Shakopee
	Abramson, Burton I.	Minneapolis
*	Abramson, Milton	Minneapolis
	Abullarade, Jose A.	Minneapolis
	Abuzzahab, Faruk S.	Minneapolis
	Adair, Albert F., Jr.	St. Paul
	Adams, George L.	Minneapolis
	Adams, Harold R.	St. Paul
	Adams, Patrick J.	Burnsville
	Adams, Richard I.	Minneapolis
	Adcock, Leon L.	St. Paul
	Adcock, Madeline S.	St. Paul
	Adicoff, Arnold	Minneapolis
	Adkins, C. Douglas	Minneapolis
	Adkins, James T.	Coon Rapids
	Adson, Martin A.	Rochester
	Affeldt, Daniel E.	Kasson
	Aga, John J.	Brainerd
	Agee, Andrew R.	Golden Valley
	Agustsson, Hreidar	Minneapolis
	Ahern, Eugene E.	Minneapolis
†	Ahlfs, Jacob J.	Ft. Lauderdale, FL
	Ahlstrom, Robert C.	Minnetonka
	Ahmann, David L.	Rochester
	Ahola, Kenneth E.	Hibbing
	Ahrens, Curtis F.	Duluth
	Ahrens, Robert M.	St. Paul
	Akbar, Sajady	Minneapolis
	Akhaven, Traz	Alexandria
	Akins, Willard M.	Red Wing
	Aksoy, Mustafa	St. Paul
	Alari, Heino	Excelsior
	Alden, Charles W.	Sauk Rapids
	Alden, John F.	St. Paul
†	Aling, Charles A.	Minneapolis
	Alkon, Ellen	Minneapolis
£	Allan, James W.	St. Paul
	Allen, George L.	Rochester
	Allen, James R.	Minneapolis
	Allen, John H.	Montevideo
§	Alexander, Gordon L.	Hopkins
	Aexander, Paul J.	Hibbing
	Allison, David D.	Litchfield
	Alt, Thomas H.	Minneapolis
	Alter, Milton	Minneapolis
	Altman, Robert L.	St. Paul
	Alton, Donald G.	St. Paul
	Amatuzio, Donald S.	Minneapolis
	Amerongen, Werner W.	St. Paul
	Amra, Waleed	Chaska
	Amren, Don P.	Minneapolis
	Anderegg, Alfred F.	Minneapolis
	Andersen, Horace J.	Winona
	Andersen, Howard A.	Rochester
	Andersen, James G.	Minneapolis
	Andersen, Robert C.	Minneapolis
	Anderson, Arden O.	Brainerd
	Anderson, Arnold S.	Minneapolis
	Anderson, Carl F.	Rochester
	Anderson, Chester A.	Hector
	Anderson, Chester A.	Madison
	Anderson, Dale L.	St. Paul
	Anderson, Darrel R.	Hopkins
	Anderson, David M.	Minneapolis
	Anderson, David P., Jr.	Austin
	Anderson, David W.	St. Paul
†	Anderson, Ernest R.	Minneapolis
	Anderson, Frank J.	Minneapolis
	Anderson, Franklin C.	Owatonna
	Anderson, Harold J.	Austin
	Anderson, James J.	St. Paul
	Anderson, Jo E.	LeSueur
	Anderson, John A.	Minneapolis
	Anderson, John R.	Minneapolis
	Anderson, John W.	Blue Earth
†	Anderson, Karl W.	Excelsior
	Anderson, Margaret C.	St. Paul
†	Anderson, Mark J.	Sun City, AZ
	Anderson, Markham J., Jr.	Rochester
#	Anderson, Michael D.	Rochester
	Anderson, Milton W.	Rochester
	Anderson, Oscar D.	Mankato
	Anderson, Quentin N.	Minneapolis
	Anderson, Richard W.	St. Paul
	Anderson, Richard W.	Minneapolis
	Anderson, Roger E.	Minneapolis
	Anderson, Roger L.	Minneapolis
	Anderson, Russell H.	Virginia
†	Anderson, U. Schuyler	Ft. Snelling
	Anderson, W. Robert	Minneapolis
	Anderson, Waldo P.	Buffalo
	Anderson, Wallace E.	Minneapolis
	Anderson, William H.	Minneapolis
	Anderson, William T.	Minneapolis
	Andre, James C.	Minneapolis
†	Andreassen, Einar C.	Minneapolis
	Andreassen, Rolf L.	Minneapolis
	Andresen, Karl d'A	Minneapolis
	Ankner, Frank J.	Minneapolis
	Anonsen, Richard E.	Minneapolis
	Ansari, Azam	Minneapolis
	Anselment, Lois A.	Excelsior
	Antolak, Stanley J., Jr.	St. Paul
	Antonelli, Jordan J.	Hibbing
	Antonow, Arthur M.	Virginia
#	Appelstein, Bruce	Chicopee, MA
	Arenson, Jeffrey A.	Minneapolis
	Arey, Lane	Minneapolis
	Arhelger, Stuart W.	Minneapolis
	Arlander, Clarence E.	Minneapolis
	Arlander, Thomas R.	Minneapolis
	Arling, Leonard S.	Minneapolis
	Arms, James J.	Minneapolis
	Armstrong, Byron H.	Minneapolis
	Armstrong, Ralph S.	Winnebago

	Arnar, Orn	Minneapolis
†	Arndt, Harry W.	Detroit Lakes
	Arnesen, John F.	Owatonna
	Arnesen, Paul M.	Mankato
†	Arnold, Ann W.	Stillwater
	Arnold, Neil S.	St. Paul
£	Arnold, Patrick N.	St. Paul
	Arnold, Thomas B.	Minneapolis
	Arny, Frederick D.	St. Paul
†	Arny, Frederick P.	St. Paul
	Arny, Peter D.	St. Paul
£	Aruquete, Jose	Chicago, IL
£	Ascough, Bruce M.	Panorama City, CA
	Ashmore, Herbert C.	St. Paul
	Asp, Donald S.	St. Paul
	Asta, Joseph J.	Duluth
†	Athens, Alvin G.	Santa Barbara, CA
	Atmore, William G.	Duluth
£	Atwell, David T.	Rochester
	Aufderheide, Arthur C.	Duluth
*	Aughenbaugh, John W.	Minneapolis
	Aulick, Ernest J.	Paynesville
	Ault, Lynn L.	St. Paul
	Auran, David B.	St. Paul
	Aurelius, J. Richards	St. Paul
	Ausman, Duane R.	St. Paul
	Ausman, James I.	Minneapolis
	Austrian, Sol	St. Paul
	Autrey, William A.	St. Cloud
	Avant, Robert F.	Minneapolis
	Avren, Barbara L.	Virginia
	Ayala, Giavanna F.	Minneapolis
	Azad, Manouchehr M.	Minneapolis
	Azzam, Fouad G.	Minneapolis

B

	Baab, Gary H.	St. Paul
	Babb, Frank S.	St. Paul
	Bach, Jerome M.	Minneapolis
£	Bachand, Romeo T., Jr.	Rochester
	Bachmann, Sigrid A.	St. Paul
	Backus, Byron C.	Cloquet
	Backus, Lloyd B.	Minneapolis
	Backus, Reno E.	Minneapolis
†	Backus, Reno W.	Cloquet
	Bader, J. L.	Slayton
	Baggenstoss, Archie H.	Rochester
	Baggenstoss, Gary A.	Minneapolis
	Baggenstoss, Osmond J.	Minneapolis
	Bagley, Charles M.	Duluth
	Bagley, Elizabeth C.	Duluth
	Bagley, Russell W.	Minneapolis
	Bagnoli, Thomas C.	St. Paul
	Bah, Merle C.	St. Paul
	Baich, Velemir M.	Coleraine
	Bailey, Walter J.	St. Paul
	Bailly, Richard C.	Camp Lejeune, NC
†	Bair, Hugo L.	Rochester
	Baird, Raymond L.	Reno, NV
¶	Bajec, Dusan	Poljane, Yugoslavia
	Baken, Melvin P., Jr.	Minneapolis
	Baker, Abe B.	Minneapolis
	Baker, C. Camak	Minneapolis
	Baker, Chilton R., Jr.	St. Paul
	Baker, Daniel R.	Anoka
†	Baker, George S.	Rochester
	Baker, Hillier L., Jr.	Rochester
	Baker, Jeannette L.	Fergus Falls
	Baker, Lowell H.	Minneapolis
	Baker, Milton E.	Minneapolis
	Bakke, Arnold C.	Minneapolis
	Bakkila, Henry E.	Duluth
	Balce, Regino V.	St. Paul
	Balcos, Emmanuel G.	Minneapolis
	Balderson, Robert P.	Grand Rapids
	Balfour, William M.	Lawrence, KS
*†	Balkin, Samuel G.	Minneapolis
	Balkins, John W.	Minneapolis
	Ballantine, Jerome J.	St. Cloud
	Balmer, Albert I.	Duluth
	Balogh, Charles J.	Minneapolis
	Bancroft, Burton R., Jr.	St. Cloud
	Bandt, Calvin M.	Minneapolis
	Banfield, Frederick	Rochester
†	Bank, Harry E.	Minneapolis
	Banner, Edward A.	Rochester
	Banovetz, John D.	Minneapolis
	Baraga, Anthony R.	Hibbing
	Barber, Tracy E.	Austin
£	Bardsley, William T. Y.	Rochester
	Barnes, M. J.	Battle Lake
	Barnes, Richard E.	Aurora
	Barnett, Robert M.	Minneapolis
	Barno, Alex	Minneapolis
	Barr, Lowell C.	Albert Lea
	Barr, Lowell W.	Albert Lea
	Barr, Maxwell M.	Minneapolis
£	Barrett, David M.	Rochester
	Barrett, Earl E.	Duluth
	Barrett, Patrick J.	Minneapolis
	Barron, Jesse J.	Minneapolis
†	Barron, Moses	Beverly Hills, CA
£	Barron, Stephen E.	Rochester
	Barry, George J.	Minneapolis
	Barry, Maurice J., Jr.	Rochester
	Bart, Bruce J.	Minneapolis
*	Bartholdt, H. Peter	Mora
	Bartholomew, Lloyd G.	Rochester
	Bartzen, Peter J.	Duluth
	Basinger, Harold P.	Windom
†	Basinger, Homer P.	Windom
	Bastron, James A.	Rochester
	Batdorf, B. Niles	Mankato
	Bateman, Clarence V.	Fergus Falls
	Bauer, Eugene L.	St. Paul
	Bauman, John C.	Foley
	Baumgartner, C. John	Minneapolis
	Baumgartner, Florian H.	Albany
	Bayrd, Edwin D.	Rochester
	Beabout, John W.	Rochester
	Beach, Northrop	Minneapolis
	Beahrs, Oliver H.	Rochester
	Bealka, Neil M.	Stillwater
	Bean, Charles N.	Waconia
	Beard, Archibald H., Jr.	Minneapolis
	Beaton, J. Gordon	Northfield

#	Bechamps, Gerald J.	Winchester, VA
	Beck, Charles J.	No. St. Paul
#	Beckenbaugh, Robert D.	Fort Hood, TX
	Becker, Frederic T.	Duluth
	Beckering, Roland G.	Edgerton
£	Beckerman, Stephen B.	Rochester
#	Beckley, James M.	Ft. Hood TX
	Becklund, Roger W.	Minneapolis
	Beckman, Donovan L.	St. Paul
	Beecher, Lee H.	Minneapolis
	Beek, Harvey O.	St. Paul
	Beeman, John A.	Minneapolis
	Beer, John J.	St. Paul
	Behr, Orlo K.	Crookston
†	Beirstein, Samuel	San Diego, CA
†	Beiswanger, Richard H.	Edina
	Belau, Paul G.	Rochester
	Belcher, Royden A.	Little Falls
§	Bell, Clifford	Blue Earth
	Bell, Donald C.	Minneapolis
	Bellomo, James	St. Paul
	Bellomo, John	Fairmont
	Bellville, Titus P.	Minneapolis
	Belshe, Joseph	St. Cloud
	Belsito, Alphonso A.	St. Paul
	Belz, Reinmar	St. Paul
	Belzer, Meyer S.	Minneapolis
	Bendel, Richard P.	Minneapolis
	Bendel, William L., Jr.	Coon Rapids
†	Bendix, Lester H.	Annandale
	Benesh, Louis A.	Minneapolis
£	Benjamin, Charles I.	St. Paul
	Benjamin, Edwin G.	Minneapolis
	Benjamin, Harold G.	Minneapolis
	Benjamin, Richard D.	Minneapolis
	Benjamin, Robert B.	Minneapolis
	Benjamin, Roger J.	Owatonna
†	Benjamin, Walter G.	Pipestone
	Bennett, Clayton J.	Rochester
	Bennington, Judith A.	Chaska
	Bensman, Alan S.	Minneapolis
	Benson, Ellis S.	Minneapolis
	Bentz, Herman D.	Anoka
	Bentzin, C. K.	Monticello
†	Bepko, Marie K.	Cloquet
	Berestka, Stephen J.	Minneapolis
	Berg, Arnold M.	Thief River Falls
	Berg, Clinton C.	Excelsior
	Berg, John H., Jr.	New Prague
*†	Bergan, Otto	Clinton
	Bergan, Richard M.	Grand Rapids
	Bergan, Robert O.	Duluth
	Berge, Kenneth G.	Rochester
	Berger, Alex G.	Minneapolis
	Berger, Phil R.	St. Cloud
	Bergersen, Dean H.	Arlington
	Bergh, Allen V.	St. Paul
	Bergh, George S.	Minneapolis
	Bergh, Solveig M.	Minneapolis
	Berglund, Alvin E.	Cambridge
	Berglund, Eldon B.	Minneapolis
	Bergquist, James R.	Minneapolis
	Bergstedt, John E., Jr.	St. Paul
	Bergstrom, John G.	Cokato
	Bergstrom, Ralph W., Jr.	Maple Plain
	Bergstrom, William J.	Minneapolis
†	Berkman, John M.	Rochester
*†	Berkwitz, Nathaniel J.	Minneapolis
	Berman, David A.	Minneapolis
	Berman, Reuben	Minneapolis
	Bernal, Jorge	Virginia
	Bernier, Merrill J.	No. St. Paul
	Bernstein, Dorothy M.	Minneapolis
	Bernstein, Irving C.	Minneapolis
†	Bernstein, William C.	St. Paul
	Berris, Harold	Minneapolis
	Berry, Ronald N.	Minneapolis
£	Bert, Jeffrey K.	Rochester
	Berzins, Rainis	Minneapolis
†	Bessesen, Alfred N.	Minneapolis
	Beuning, John B.	St. Cloud
	Bevis, William D.	Minneapolis
	Bhatnagar, Prakhar	Plymouth
†	Bianco, Anthony J.	Vero Beach, FL
	Bianco, Anthony J., Jr.	Rochester
	Bickel, William H.	Rochester
§	Biebl, Jonathan H.	Richfield
	Bieger, R. Cyril	Minneapolis
	Biery, M. Barbara	Minneapolis
†	Bieter, Raymond N.	Minneapolis
	Bieter, Thomas G.	St. Paul
	Bigler, Earl E.	Perham
	Bigler, Ivan E.	Perham
	Bilgutay, Aydin M.	Minneapolis
	Bilka, Paul J.	Minneapolis
	Billings, Harry H.	Red Wing
	Billman, Herbert R.	Minneapolis
*	Biltz, John F.	Red Wing
	Binder, Manuel R.	Minneapolis
#	Bingham, George C.	Pensacola, FL
	Birkebak, Roland C.	St. Paul
	Birkemeyer, Eugene J.	Worthington
	Birkey, Thomas G.	Montevideo
	Bisel, Harry F.	Rochester
†	Bishop, James R.	Minnetonka
	Bissinger, Lester L.	Brainerd
	Bittick, Wilbur H.	Minneapolis
	Bjornson, Robert G. B.	St. Paul
	Black, B. Marden	Rochester
	Black, Leo F.	Rochester
£	Black, Steven B.	Rochester
	Black, William A.	New Ulm
	Blackard, Clyde E.	Minneapolis
	Blackburn, Henry W., Jr.	St. Paul
	Blake, Allan J.	Hopkins
§	Blake, David F.	Hopkins
	Blake, James A.	Hopkins
	Blake, Paul S.	Minneapolis
£	Blanco-Benavides, Roberto	Rochester
	Bland, Charles S.	Minneapolis
	Bloedel, Traugott J.	Osseo
	Blomberg, Robert D.	Minneapolis
	Blomberg, William R.	St. Paul
	Bloom, David	Minneapolis
†	Bloom, Joseph	Pompano Beach, FL
	Bloom, Norman B.	Minneapolis
	Bloom, Stephen H	Duluth
	Blum, Clifford J.	Duluth
	Blumberg, Henry B.	St. Paul
	Blumenthal, Malcolm N.	Minneapolis
	Blumer, Arlo R.	Albert Lea
	Boardman, Dalmon V.	Greeley, CO
	Boardman, Peter J.	Wayzata
	Boardman, William J.	Minneapolis
†	Bock, Rolland A.	St. Paul
	Bocklage, Joseph F.	Minneapolis

	Boecker, Bernhard	Duluth
	Bofenkamp, Benjamin	Minneapolis
†	Bofenkamp, Ferdinand W.	Luverne
	Bohrer, James A.	Austin
†	Boies, Lawrence R.	Hopkins
	Boies, Lawrence R., Jr.	St. Paul
*	Boline, Clifford A.	Battle Lake
	Boller, Max A.	Minneapolis
	Bologna, Camillo V.	Moorhead
	Bolz, J. Arnold	Grand Rapids
†	Boman, Paul G.	Duluth
	Boman, Peter L.	Duluth
	Bonewell, George W.	Minneapolis
	Bonello, Frank J.	St. Paul
	Bonner, John L.	Grand Rapids
	Boody, George	Cambridge
	Boone, Ervin S.	Luverne
#	Boren, Gregory C.	Ft. Hood, TX
†£	Borgerson, Arthur H.	Long Prairie
	Borgerson, M. A.	Hanley Falls
†	Borman, Chauncey N.	Minneapolis
	Borowicz, Leonard A.	Minneapolis
	Borrud, Chester C.	Anoka
	Bosch, Otto K.	St. Paul
	Bosland, Howard G.	Ida Grove, IA
†	Bottolfson, B. T.	Moorhead
†	Bouma, Lewis R.	St. Paul
	Bouquet, Bertram J.	Wabasha
	Bouthilet, Florence J.	Minneapolis
†	Bowers, Gordon G.	Excelsior
	Bowers, Robert N.	Lake City
	Bowlin, Paul F.	Minneapolis
†	Boyd, David A., Jr.	Rochester
	Boyd, Frank E.	Pipestone
	Boyer, Samuel H.	Duluth
	Boyle, Francis J.	Springfield
†	Boynton, Ruth E.	Miami, FL
	Boysen, Alexander	Bemidji
†	Boysen, Herbert	Madelia
†	Boyum, Allan J.	Minneapolis
	Bozanich, Milosh S.	St. Cloud
†	Braasch, William F.	Rochester
†	Brabec, Paul F.	Hastings
	Brace, Ray I.	Willmar
	Bradford, David S.	Minneapolis
	Bradley, Jeanne B.	Minneapolis
	Bradley, John G.	Minneapolis
	Bradley, William E.	Minneapolis
	Brage, John R.	Minneapolis
	Brainard, John B.	St. Paul
	Brakke, Mark H.	Coon Rapids
	Brandenburg Robert O.	Rochester
	Brandt, Donald E.	St. Paul
	Brandt, Henry E.	Minneapolis
	Bransford, Paul W.	Minneapolis
	Bratholdt, James W.	Watertown
†	Bratrud, Edward	Alexandria
	Brattensborg, Henry J.	St. Cloud
	Brauer, William W.	Minneapolis
	Braun, Ohrmundt C.	Grand Rapids
£	Braun, Donald P.	Rochester
	Braun, Rene	Minneapolis
	Bray, Jerome L.	Thief River Falls
	Bray, Philip N.	Duluth
£	Breadon, George E.	Rochester
	Breen, John J.	St. Paul
	Breitenbucher, Robert B.	Minneapolis
#	Breivis, James S.	Spokane, WA
†	Brekke, Harvey J.	Minneapolis
	Brenk, Paul E.	Detroit Lakes
	Brennan, Joseph G.	Minneapolis
	Brennom, William S.	St. Paul
	Brettingen, Larry J.	Mora
	Bretzke, Carl O.	Hutchinson
#	Brewster, Robert C.	Rochester
	Briggs, Thomas G.	White Bear Lake
	Brigham, Charles F., Jr.	St. Cloud
	Brill, Alice K.	Minneapolis
	Brink, Adlai A.	Baudette
	Brink, Donald M.	Hutchinson
	Brinton, Edward H.	Rochester
	Briones, Bienvenido R.	Hopkins
£	Broadie, Tomas E.	St. Paul
	Brockberg, Daryl G.	St. Paul
	Brockberg, James A.	St. Paul
	Brodhun, John C.	Rochester
†	Brodie, Walter D.	St. Paul
	Brodsky, Ivan L.	Minneapolis
	Broker, Henry M.	St. Cloud
	Broman, Harold R.. Jr.	No. St. Paul
	Bromen, Kenneth A.	Duluth
	Bromer, Michael D.	Minneapolis
	Brooker, Warren J.	Duluth
†	Brooks, Charles N.	Wayzata
†	Brown, Alex E.	Bradenton, FL
	Brown, Arnold L.	Rochester
	Brown, Charles T.	St. Paul
	Brown, Christopher J.	St. Paul
	Brown, Cyrus C., Jr.	Duluth
	Brown, David M.	Minneapolis
	Brown, Frank T.	St. Cloud
	Brown, Glenn W.	Halstad
	Brown, Hector M.	St. Paul
	Brown, Henry A.	Rochester
	Brown, James E., Jr.	St. Paul
	Brown, James P.	St. Paul
	Brown, James R.	Crookston
	Brown, Joe R.	Rochester
	Brown, John H.	Minneapolis
	Brown, John M.	St. Paul
	Brown, Larry R.	Rochester
†	Brown, Philip W.	Rochester
	Brown, Russell T.	Browerville
	Brown, Warwick L.	Rochester
	Brown, William D., Jr.	Minneapolis
£	Brownfield, James A.	Minneapolis
	Brubaker, Richard F.	Rochester
	Bruhl, Heinz H.	Faribault
	Bruhl, Martin G.	St. Paul
	Bruns, Donald L.	Red Wing
†	Brusegard, James F.	Red Wing
	Bucher, Foster D.	Starbuck
¶	Buchholz, Roger M.	Rochester
	Buchstein, Harold F.	Minneapolis
	Buchwald, Henry	Minneapolis
†	Buck, Frederick H.	Shakopee
	Buckley, Joseph J.	Minneapolis
†	Buckley, Robert P.	Duluth
	Budd, Frank W.	Duluth
	Buege, William	Albert Lea
	Buesgens, Ralph H.	Waterville
	Bugby, Robert D.	Minneapolis
	Bugenstein, Robert H.	Minneapolis
†	Buie, Louis A.	Rochester
	Buie, Louis A., Jr.	Minneapolis
	Bulinski, Theodore J.	St. Paul
	Bulluck, Matthew H.	Duluth

	Bundt, Robert E.	Minneapolis
	Bunker, Bevan W.	Anoka
	Bunnell, Harris F.	Winona
	Buran, David J.	Minneapolis
	Burchell, Howard B.	Minneapolis
	Buresh, Kenneth L.	Owatonna
	Burgert, E. O., Jr.	Rochester
£	Burgher, Louis W.	Rochester
	Burich, Harry F.	Rochester
	Burke, Edmund C.	Rochester
	Burkholder, Dayton D.	Anoka
	Burkland, Carl E.	New Prague
	Burklund, Edwin C.	St. Paul
	Burlingame, David A.	St. Paul
	Burman, Richard E.	Minneapolis
	Burmaster, Robert W.	St. Cloud
	Burnett, Joseph W.	New Ulm
	Burnham, Wesley H.	Minneapolis
†	Burns, Catherine	Excelsior
	Burns, James F.	Albert Lea
	Burns, John M.	St. Paul
†	Burns, M. A.	Edina
£	Burns, Sheldon	St. Paul
	Burseth, Edgar C.	Mora
	Burton, J. Richard	St. Paul
	Burton, Thomas P.	Minneapolis
#	Bush, David J.	Biloxi, MI
	Bush, Robert P.	St. Paul
	Bustos, Manual	St. Paul
	Butler, Brooks A.	St. Paul
	Butler, John K.	Cloquet
	Butt, Hugh R.	Rochester
	Butwinick, Conrad S.	St. Paul
†	Butzer, John A.	Mankato
£	Buzanowski, Krystina	Rochester
	Byrne, William J.	St. Paul

C

†	Cable, Morris L.	Minneapolis
†	Cabot, Clyde M.	Ft. Lauderdale, FL
	Cadbury, Jane B.	Mankato
§	Cadwell, Frank	Minneapolis
	Cady, Timothy J.	Buffalo
	Cain, Clark L.	St. Paul
	Cain, James C.	Rochester
	Cain, James H.	Alexandria
	Cairns, Robert J.	Redwood Falls
	Calin, S. Hartley	Minneapolis
	Callahan, John A.	Rochester
	Cameron, Alan J.	Rochester
	Cameron, Bruce P.	Minneapolis
*†	Cameron, Isabell L.	Minneapolis
	Camp, Ray J.	Madison
	Campaigne, Robert J.	Duluth
	Campbell, Craig W.	Duluth
	Campbell, Denis V.	Minneapolis
	Campbell, Donald C.	Rochester
	Campbell, Malcolm K.	Rochester
	Campbell, Marilyn R. M.	Minneapolis
†	Campbell, Orwood J.	Tucson, AZ
	Campbell, Ronald G.	Minneapolis
	Campion, Brian C.	St. Paul
	Campos, Amador C.	Eveleth
	Canfield, John L.	Chaska
	Canine, James L.	Minneapolis
£	Cannon, Patrick J.	Rochester
	Canto, Jose D.	So. St. Paul
	Capistrant, Terrance D.	St. Paul
	Card, William H.	Minneapolis
	Cardle, George E.	Brainerd
	Cardle, James G.	Minneapolis
	Cardle, John B.	Minneapolis
	Carlander, Lester W.	Minneapolis
	Carley, Richard B.	St. Paul
	Carlon, Donald L.	Moorhead
	Carlson, Carl E.	Alexandria
	Carlson, Charles V.	Mound
	Carlson, Clifford A.	Minneapolis
	Carlson, Curtis H.	Minneapolis
	Carlson, David J.	Minneapolis
	Carlson, Harley C.	Rochester
	Carlson, Homer J.	Pelican Rapids
	Carlson, John V.	Westbrook
†	Carlson, Lawrence	Minneapolis
	Carlson, Lloyd E.	Worthington
£	Carlson, Richard A.	Rochester
	Carlson, Richard W.	Minneapolis
	Carlson, Vernon J.	Moorhead
	Carney, Francoise	Rochester
	Carney, John A.	Rochester
	Carr, David T.	Rochester
	Carr, William J.	Minneapolis
	Carrier, Thomas C.	Edina
	Carryer, Haddon M.	Rochester
	Carson, John F.	Aitkin
	Carter, Darrell J.	Granite Falls
	Carter, Earl T.	Rochester
	Carter, Kenneth R.	Granite Falls
£	Carter, M. Gary	Rochester
	Carter, Robert E.	Duluth
	Carter, Robert G.	Thief River Falls
	Carthy, Frank J.	New Ulm
	Caspers, Carl G.	Minneapolis
	Casperson, Tom	Winona
	Cass, Alexander S.	St. Paul
	Cass, Irene	St. Paul
	Cassell, Wilfred A.	St. Paul
	Catlin, Theodore J.	Buffalo
	Cauble, Charles F.	Minneapolis
	Cava, Eugenio F.	Fridley
†	Cavanor, Frank T.	Minneapolis
	Cavert, H. Mead	Minneapolis
	Cedarleaf, Cherry B.	White Bear Lake
	Cedarleaf, Shirley J.	Edina
	Ceder, Elmer T.	Minneapolis
	Cella, Joseph A.	Minneapolis
	Ceplecha, Stanley F.	Rochester
	Cervenka, Charles F.	New Prague
	Cervenka, John D.	New Prague
	Cesnik, Robert J.	Sauk Rapids
	Chadbourn, Wayne A.	Minneapolis
	Chalgren, William S.	Mankato
	Challman, S. Alan	Minneapolis
	Chally, Cecil H.	Minneapolis
£	Chiavetta, Stephen V. Jr.	Rochester
	Chandler, William M.	Minneapolis
*†	Chatterton, Carl C.	St. Paul
	Chawla, Ramesh C.	St. Cloud
	Chedister, Charles R.	Minneapolis
	Chermak, Francis G.	Phoenix, AZ

	Chervenak, William A.	St. Paul
	Chesebro, James H.	Rochester
	Chesler, Merrill D.	Minneapolis
£	Chiavetta, Stephen V., Jr.	Rochester
	Child, Sherman B.	Minneapolis
	Childs, Donald S., Jr.	Rochester
	Chilgren, Keith V.	St. Paul
	Chisholm, Tague C.	Minneapolis
	Chizek, David	St. Paul
	Choithani, C. M.	Crookston
	Choithani, H. C.	Crookston
	Chou, Shelley N.	Minneapolis
	Christensen, Clarence H.	Duluth
†	Christensen, Eli E.	Winona
	Christensen, Llewellyn E.	Minneapolis
	Christensen, Norman A.	Rochester
£	Christensen, Robert D.	Rochester
£	Christenson, Carl E.	Brighton
	Christenson, Leland R.	Minneapolis
	Christgau, Roger A.	Minneapolis
	Christian, William L.	Minneapolis
	Christiana, Richard L.	Rochester
	Christiansen, Harold A.	Jackson
	Chua, Marianito S.	White Bear Lake
#	Chumbley, Lee C.	Patuxent River, MD
	Chunn, Stanley S.	Willmar
	Church, Gerald E.	Two Harbors
	Churchill, Jane	Park Rapids
	Cich, John A.	Minneapolis
£	Cintora, Ismar	Minneapolis
	Ciriacy, Edward W.	Minneapolis
	Clapp, Hubert D.	Crookston
†	Clark, Edward C.	San Francisco, CA
	Clark, Elizabeth A. (Mrs. Halbert)	Duluth
†	Clark, Harry B.	St. Cloud
	Clark, Malcolm D.	Minneapolis
£	Clark, Paul S.	Rochester
	Clark, Robert S.	Minneapolis
	Clark, W. Bruce	St. Paul
	Clarke, Dean T.	Faribault
	Clarke, John W.	Waconia
	Clay, Lyman B.	Minneapolis
*	Clifford, George W.	Alexandria
	Clifford, Thomas M.	Silver Bay
†	Clifton, Theodore A.	Hollywood, FL
	Cline, David W.	Minneapolis
	Close, Gerald A.	Glencoe
	Closuit, Frederick	Aitkin
	Cochrane, Byron B.	St. Paul
	Cochrane, Ray F.	Minneapolis
	Coddon, Walter D.	St. Paul
	Cody, D. Thane	Rochester
£	Cody, Michael C.	Rochester
	Coe, John I.	Minneapolis
	Coe, Robert O.	Virginia
	Cohen, Bernard A.	Minneapolis
	Cohen, Ephraim B.	Minneapolis
	Cohen, Henry W.	Wayzata
*†	Cohen, Sumner S.	Minneapolis
	Coifman, Robert E.	Minneapolis
	Colago, Victor M.	Browns Valley
	Colby, Malcolm Y., Jr.	Rochester
†	Colby, Woodard L.	St. Paul
	Cole, George A.	Albert Lea
	Cole, James S.	Minneapolis
	Cole, Wallace H.	St. Paul
	Coleman, John B.	St. Paul
#	Coleman, Robert L.	Whiteman AFB, MO
#	Coleman, Thomas P.	Minneapolis
	Coll, James J.	Duluth
	Collinge, James H.	Detroit Lakes
	Collins, Roger T.	Duluth
	Colliton, Patrick A.	Moorhead
	Colman, Edward L.	Fergus Falls
	Colosey, Fredericks	Virginia
	Colton, Roger S.	St. Paul
	Comfort, Thomas H.	St. Paul
	Conlon, Daniel C.	Minneapolis
£	Conn, Richard L.	Rochester
	Connolly, Coleman J.	St. Paul
	Connolly, Joseph P.	So. St. Paul
†	Connor, Charles E.	St. Paul
	Coombs, Carl H.	Cass Lake
	Coomes, Michael	Montevideo
	Cooper, Auran M.	Cleveland, OH
	Cooper, Charles C.	Moose Lake
	Cooper, Jack M.	St. Paul
	Cooper, John P.	Minneapolis
	Cooper, Robert R.	Minneapolis
	Cooper, Talbert	Rochester
#	Cooperman, Avram M.	Wichita Falls, TX
	Cope, Hershel B.	Virginia
†	Corbin, Kendall B.	Sarasota, FL
†	Corniea, Albert D.	Minneapolis
	Correa, Dale H.	Minneapolis
	Corrigan, Cyril J.	Rochester
	Corson, Wilfred A.	Minneapolis
£	Cortese, Denis A.	Rochester
	Cortez, Daniel P.	Minneapolis
	Cosgriff, James A., Jr.	Olivia
	Cotton, Gerald E.	Duluth
	Coulter, Harold E.	Minneapolis
#	Courteau, Robert D.	Ginelo, Rhodesia
	Coventry, Markham B.	Rochester
	Covey, Kenneth W.	Moorhead
†	Cowan, Donald W.	Minneapolis
	Cowan, Gary A.	Duluth
	Cowan, George M.	Duluth
£	Cowger, Robert C.	Farmington
	Cox, Milton J.	Duluth
	Cox, Russell L.	Spirit Lake, Iowa
	Coy, Douglas J.	Grand Rapids
	Craig, David M.	St. Paul
	Craig, M. Elizabeth	Minneapolis
	Cram, Barclay M.	St. Paul
	Cramer, Glen G.	New Brighton
†	Cranmer, Richard R.	Laguna Hills, CA
†	Cranston, Robert W.	Minneapolis
	Creevy, Charles D.	Minneapolis
£	Creme, Joseph J.	Minneapolis
	Creps, James R.	Duluth
	Cress, Thomas L.	St. Cloud
	Crislip, George D.	Waconia
	Croissant, Raymond C.	Minneapolis
†	Cronwell, Bernhard J.	Austin
†	Crow, Earl R.	Minnetonka
	Crow, George M.	International Falls
£	Crowder, David F.	Rochester
	Crowley, James H.	St. Paul
	Crowley, Leonard V.	Minneapolis
	Crudo, Vincent D.	St. Paul
	Crum, Arthur Z.	St. Paul
	Crutchfield, Charles E.	St. Paul
	Crutchfield, Susan E.	St. Paul
§	Cruz, Baltasar	St. Paul
	Cruz, Waldemar F.	Minneapolis
£	Csir, Floyd M.	Rochester
	Cuderman, Bart S.	Duluth

	Cullado, Andrionico F.	Minneapolis
	Cullen, Robert M.	Elmore
	Culligan, David E.	St. Paul
	Culligan, John A.	St. Paul
	Culligan, Leo C.	Minneapolis
	Culp, Clyde E.	Rochester
§	Culp, Kim Steven	Minneapolis
	Culp, Ormond S.	Rochester
	Culver, Lucian G.	St. Paul
	Cumming, Edward D.	St. Paul
	Cumming, Robert J.	St. Cloud
	Cundy, Donald T.	Minneapolis
	Cupps, Roger E.	Rochester
	Curran, John P.	Minneapolis
	Cushing, Richard T.	Minneapolis
†	Cutts, George	Minneapolis

D

	Dagg, Earl	Thief River Falls
	Daggett, Donald R.	Minneapolis
	Dahl, James C.	Minneapolis
*†	Dahl, John A.	Excelsior
	Dahlin, David C.	Rochester
	Dahlquist, LaRue	St. Cloud
	Dahlstrom, Donald D.	Minneapolis
	Dailey, John C.	Duluth
	Dale, Allan J. D.	Rochester
	Dale, Les N.	Hastings
	Daly, Alfred E.	St. Paul
	Damberg, Sheldon W.	St. Paul
†	Daniel, Donald H.	Wayzata
	Daniels, Clarke G.	Minneapolis
	Danielson, Lennox	Litchfield
	Danoff, David	Minneapolis
	Danyluk, Michael	Minneapolis
	Dargay, Cyril P.	Minneapolis
	Daugherty, Guy W.	Rochester
	Daumann, Roy F.	Minneapolis
£	Dauphine, Richard T.	Rochester
	Davenport, Jay A.	Virginia
	David, Reuben	Hopkins
	Davidson, A. Dale	Duluth
	Davidson, Duane J.	Thief River Falls
£	Davidson, Michael J.	Rochester
†	Davis, Austin C.	Pompano Beach, FL
	Davis, Curtis E.	Minneapolis
£	Davis, David L.	Huntington Beach, CA
	Davis, Edward V.	St. Paul
	Davis, Eunice A.	St. Paul
	Davis, George D.	Rochester
†	Davis, Lloyd T.	Wadena
	Davis, Luther F.	Fargo, ND
	Davis, Michael W.	Minneapolis
	Davis, Raymond D.	Stockton, CA
	Davis, Thomas H.	Minneapolis
	Davis, William E.	St. Paul
	Davis, William I.	Moose Lake
	Davis, Zev	Rochester
	Dawson, Lorin D.	Worthington
	Dawson, W. John, Jr.	Minneapolis
	Dearing, William H.	Rochester
	Deason, Keith B.	Chisago City
	Deaton, Burrell H.	Minneapolis
¶	DeBus, Robert L.	Rochester
	DeCeseare, Ronald E.	Edina
	Decker, Charles W.	Hibbing
	Decker, David G.	Rochester
£	DeCourcy, Donald M., Jr.	Rochester
	DeCubas, Luis A.	St. Paul
	Dedeker, Kenneth L.	Minneapolis
£	Deering, Timothy B.	Rochester
	Degallier, Daniel	Winona
	DeHaan, Eddie D.	Minneapolis
	Delahunty, John R.	Red Wing
	DeLeon, Buenaventura	Stillwater
	Delmore, Jack	Roseau
	Delzell, Allen W.	Minneapolis
	De Marais, Lloyd C.	Hibbing
	Demo, Robert A.	Albert Lea
	Derauf, Donald E.	St. Paul
£	Derbenwick, Kenneth P.	Rochester
£	Derbenwick, Mary June	Rochester
	Derechin, William	St. Paul
	DeRemee, Richard A.	Rochester
	Derro, Robert A.	St. Paul
	De Santo, Lawrence W.	Rochester
	Deters, Donald C.	St. Paul
	Deutsch, Robert J.	Duluth
	DeVinck, James F.	St. Cloud
	Devine, Kenneth D.	Rochester
	Devloo, Robert A.	Rochester
	DeWeerd, James H.	Rochester
	Deweese, Joel T.	Bemidji
	Deweese, Wilford J.	Bemidji
	deWerd, Robert W.	Owatonna
	Dewey, Donald H.	Owatonna
	Dey, James W.	Waseca
	Diamond, Robert A.	Minneapolis
£	Diaz-Buxo, Jose A.	Rochester
	Dickinson, Paul B.	St. Paul
	Dickman, Roy W.	Minneapolis
	Dickson, Franklin H.	Proctor
	Didier, Edward P.	Rochester
	Diego, Benito B.	Fridley
*†	Diehl, Harold S.	New York, NY
	Diehl, James J.	Minneapolis
	Dieperink, Willem	St. Paul
	Dierker, Heinrich A.	Minneapolis
	Diessner, Ardell W.	Stillwater
	Diessner, Grant R.	Rochester
*	Dillie, Donald E.	Litchfield
	Dillenburg, Cyril J.	Crookston
	Dimants, Janis, Jr.	Minneapolis
	Dinapole, Robert P.	Rochester
	Dines, David E.	Rochester
†	Dittrich, Raymond	St. Paul
	Doan, Robert E.	Wayzata
¶	Dobbins, Donald V.	Rochester
	Dobbs, Richard L.	Duluth
	Dobler, Manfred G.	Ely
	Dobson, Mervin W.	Mankato
	Dobyns, James H.	Rochester
	Docherty, John A.	Edina
	Dockerty, Malcolm B.	Rochester
	Docksey, John W.	Willmar
	Dodds, William C.	Detroit Lakes
	Dodson, Albertus F.	Brainerd
	Doebler, Myron I.	Bagley
	Doherty, Elmer M.	New Prague
	Dokken, James H.	Windom

	Dolmage, George H.	Sun City, AZ
	Doman, Victor W.	Lakefield
§	Domino, Terry A.	St. Paul
	Doms, Vernon A.	Elbow Lake
†	Donaldson, Charles S.	St. Cloud
	Donatelle, Edward P.	Minneapolis
	Donoghue, Francis E.	Rochester
	Donovan, Daniel L.	New Brighton
	Dooley, Robert T.	St. Paul
	Doren, Austin H.	Little Fork
†	Dorge, Richard I.	Minneapolis
	Dornbach, Robert A.	Minneapolis
	Dorsey, George C., Jr.	Minneapolis
	Dorsey, William E.	Minneapolis
	Doscherholmen, Alfred	Minneapolis
	Doty, Joseph	Little Falls
	Dougan, Jerome W.	Minneapolis
	Doughman, Donald J.	Minneapolis
	Douglass, Bruce E.	Rochester
	do Vale, Joao M.	Minneapolis
	Dover, James W.	Mankato
£	Doyne, Holly L.	Minneapolis
†	Doxey, Gilbert L.	Minneapolis
	Doyle, James R.	Rochester
£	Dozois, Roger R.	Rochester
	Drage, Charles W.	Minneapolis
†	Dredge, Thomas E.	Minneapolis
	Drexler, Charles J.	Duluth
	Drexler, George W.	Blue Earth
	Dreyling, Roger A.	Eden Valley
	Drill, Frederick E.	Minneapolis
	Drill, Herman E.	Hopkins
†	Drips, Della G.	Rochester
£	Driscoll, Thomas P.	Rochester
	Drucker, Franklin G.	Bigfork
	Duane, Drake D.	Rochester
£	Du Boff, Stuart M.	Rochester
	Dubois, Julian F.	Sauk Centre
	Duerr, Eleanor E.	St. Paul
	Duffy, John L.	St. Paul
	Dummer, Donald J.	Minneapolis
	Dumonceaux, Roland G.	Edina
	Duncan, Donald A.	Minneapolis
	Duncan, Glenn W.	Rochester
	Duncan, James W.	Moorhead
	Dunham, Charles K.	St. Paul
#	Dunham, Tom R.	San Francisco, CA
	Dunkel, Thomas B.	St. Louis Park
	Dunlap, David J.	Minneapolis
†	Dunlap, Earl H.	Minneapolis
	Dunn, James P.	St. Paul
	Dunn, Robert C.	St. Paul
	Dunstan, Paul L.	Willmar
	Dupont, Joseph A.	Excelsior
	Durkin, John L.	St. Paul
†	Duryea, Willis M.	Minneapolis
	Duryea, Willis M., Jr.	Minneapolis
	Duthoy, Everette J.	St. Paul
	Dutt, Ray	St. Paul
	Duvall, Arndt J., III	St. Paul
†	Dvorak, Benjamin A.	Minneapolis
†	Dworsky, Samuel D.	Minneapolis
	Dwyer, John J.	Duluth
	Dyck, Peter J.	Rochester
	Dyer, John Allen	Rochester
£	Dyke, David R.	Rochester
	Dyrdal, Paul J.	St. Paul
†	Dysterheft, Adolf F.	Gaylord
	Dzuibinski, Emil H.	St. Cloud

E

	Earl, John R.	St. Paul
	Earl, Stephan H	Minneapolis
	Eaton, David B.	Worthington
	Eberley, Tobe S.	Benson
	Ebert, Richard V.	Minneapolis
	Eckdale, John E.	Marshall
	Eckerly, Jean R.	Minneapolis
	Eckert, Joseph F.	Mankato
	Eckman, Matthew J.	Duluth
	Eckman, Philip F.	Duluth
	Eckman, Philip L.	Duluth
	Eckman, Ralph J.	Duluth
	Eder, Walter P.	Minneapolis
	Edin, Andrew	Winona
	Edmondson, Hugh A., Jr.	Minneapolis
	Edmondson, John H.	Rochester
†	Edwards, J. Willard	St. Paul
	Edwards, Jesse E.	St. Paul
	Edwards, Laura E.	St. Paul
	Edwards, Lloyd G.	St. Paul
	Edwards, Richard B.	St. Paul
	Edwards, Thomas J.	St. Paul
†	Edwards, Walter G., Jr.	Bethesda, MD
	Edwardson, Phillip L.	St. Paul
	Eelkema, Herman H.	St. Paul
	Efteland, Myles E.	Minneapolis
	Egge, Sanford G.	Albert Lea
	Eginton, Charles T.	Fargo, ND
	Ehlen, Charles P.	St. Cloud
†	Ehrlich, S. Paul	Minneapolis
†	Eich, Matthew A.	Minneapolis
	Eichelberger, Dale L.	Willmar
	Eichenlaub, John E.	Minneapolis
	Eichhorn, Edmund P., Jr.	Minneapolis
£	Eichten, John G.	Minneapolis
	Eide, O. A.	Hancock
†	Eiden, Vera M.	Afton
	Eifrig, David E.	Minneapolis
	Eilers, Vincent E.	St. Paul
	Einzig, Mitchell J.	Wayzata
	Eisenberg, M. Michael	Minneapolis
	Eisenman, Walter	Hibbing
	Eisenstadt, William S.	Minneapolis
†	Eitel, George D.	Minneapolis
	Eklund, Carl D.	Duluth
†	Elkins, Earl C.	Rochester
	Ellerby, Richard A.	Portland, OR
	Ellertson, Leonard M.	Albert Lea
	Ellinger, Albert J.	Willmar
	Ellingson, Richard B.	Minneapolis
	Ellington, Anna L.	Minneapolis
	Ellis, Cassius M. C.	Minneapolis
	Ellis, Earl W.	Elgin
	Ellis, John C., Jr.	Minneapolis
	Ellis, Ronald W.	St. Paul
	Ellison, Evan S.	Minneapolis
	Ellwood, Paul M., Jr.	Minneapolis
	Elumba, Teodoro V.	St. Paul
	Emanuel, Karl W.	Duluth
	Emerson, Edward C.	St. Paul

Emerson, Edwin E. ....Osakis
† Emmett, John L. ....Rochester
Emmons, Patricia R. ....Vancouver, B.C.
Emmons, Robert W. ....St. Paul
† Emond, Joseph S. ....Farmington
Emond, Joseph S., Jr. ....Farmington
Emslander, Richard F. ....Rochester
*† Endress, Edward K. ....St. Paul
Engebretson, Paul ....Alexandria
Engel, Joseph P. ....Minneapolis
Engel, William L. ....Minneapolis
Engelberg, Jerry ....Fairfield, CA
† Engels, Edward P. ....Lexington, KY
Engelsgjerd, Gerald L. ....Duluth
Engelstad, Wendell P. ....Virginia
England, Rodney W. ....St. Paul
Englund, Elvin F. ....Minneapolis
Engstrom, E. Duane ....Minneapolis
Engstrom, George ....St. Peter
Engwall, Richard L. ....Minnetonka
Enroth, Oscar E. ....St. Paul
Erdal, Ove A. ....Albert Lea
Erich, John B. ....Rochester
† Erickson, Alvin O. ....Long Prairie
Erickson, Carlton ....Lindstrom
Erickson, Donald J. ....Rochester
Erickson, Donald L. ....St. Paul
Erickson, Jeffery L. ....Minneapolis
Erickson, Laurence F. ....Minneapolis
Erickson, Myron E. ....Minneapolis
Erickson, Robert L. ....Rosemount
Erickson, Vernon D. ....Grand Rapids
Ericson, John E. ....Minneapolis
Ericsson, Kermit C. ....Cambridge
Erlanson, A. Cornell ....St. Paul
£ Ersek, Robert A. ....Minneapolis
Ersfeld, Murray P. ....St. Paul
Eselius, Erik P. ....Minneapolis
Esensten, Sidney ....Minneapolis
Espeland, L. Michael ....St. Cloud
Espelien, Alan D. ....St. Cloud
Espinosa, Raul E. ....Rochester
Estrem, Ralph L. ....Fergus Falls
Estrem, Robert D. ....Fergus Falls
Ettinger, David S. ....Ft. Leavenworth, KS
Etzwiler, Donnell D. ....Minneapolis
Eusebio, Ernesto ....Minneapolis
† Evans, Edward T. ....Minneapolis
Evans, James M. ....Northfield
Evans, Leslie M. ....Sauk Rapids
Evans, Titus C. Jr. ....Rochester
Evensta, John B. ....Grand Rapids
Everhart, Clarence E., Jr. ....Minneapolis
Everly, Stephan S. ....Minneapolis
Evison, Emerson O. ....Duluth
Ewens, George B. ....Virginia
Ewing, James W. ....Bloomington

F

Faber, John E. ....Rochester
Facer, George W. ....Rochester
£ Falcone, James C. ....Rochester
Fallon, Virgil T. ....Minneapolis
Falls, John L. ....Red Wing
Fangman, James J. ....Minneapolis
Farb, Harry F. ....Minneapolis
Farber, Abigail F. ....Minneapolis
Farber, Lawrence A. ....Minneapolis
Farber, Roger E. ....Minneapolis
Farley, Harrison H. ....Minneapolis
Farr, John D. ....St. Paul
Farrell, T. Edwin ....Minneapolis
Fasbender, Herman T. ....Hastings
Fauchald, Nils, Jr. ....Red Wing
Faul, Bennie C. ....Worthington
£ Faulconer, Albert, Jr. ....Rochester
Faust, John H. ....Northfield
£ Fawcett, Arthur M. ....Renville
† Fawcett, Keith R. ....Duluth
# Fay, Thomas M. ....Oakland, CA
Fedders, Skaidrite ....Willmar
Fedor, Robert ....Willmar
Fee, John G. ....St. Paul
Fehr, Peter E. ....Minneapolis
Feigal, Gary R. ....Lake City
Feigal, William M. ....Fairmont
Feinberg, Philip ....Minneapolis
Feinberg, Samuel B. ....Minneapolis
Felder, Davitt A. ....St. Paul
Feldmann, Floyd M. ....Pompano Beach, FL
Felion, Arthur J. ....St. Paul
Fenske, Arnold W. ....Winona
* Ferguson, John N. ....St. Paul
Ferguson, Richard H. ....Rochester
Fernandez, Carlos H. ....Minneapolis
Fernandez, Rafael F., Jr. ....Minneapolis
Ferrell, Clarence R. ....Moose Lake
† Ferris, Edward O. ....Rochester
Fesenmaier, Otto B. ....Los Angeles, CA
† Fesler, Harold H. ....W. St. Paul
Fetzek, Albert D. ....Minneapolis
Feuling, John C. ....Sun City, AZ
Field, Charles S. ....Rochester
Field, Charles W. ....Hopkins
Fifer, Ellen Z. ....St. Paul
Fifer, William R. ....Minneapolis
Fifield, Malcolm M. ....Duluth
Filiatrault, L. J. ....Coon Rapids
Filipovich, Orest N. ....Minneapolis
Fingerman, David L. ....Minneapolis
Fink, Daniel L. ....St. Paul
Fink, Lawrence H. ....Bethesda, MD
† Fink, Leo W. ....Minneapolis
Fink, Robert J. ....Minneapolis
Finkelnburg, William O. ....Winona
Finkelstein, Joel ....Minneapolis
Finstad, James E. ....Minneapolis
Fiore, Joseph P. ....Rochester
Fischer, Robert F. ....St. Paul
Fish, Charles R. ....Rochester
Fisher, Don H. ....Minneapolis
Fisher, Howard W. ....Minneapolis
Fisher, Isadore I. ....Minneapolis
Fisketti, Henry ....Duluth
Fitch, Charles G. ....Worthington
Fitzsimons, William E. ....Brainerd
† Flancher, Leon H. ....Detroit Lakes
# Flanigan, Donald J. ....Englewood, CA
Flannery, Hubert F. ....St. Paul

£	Fleisher, Thomas A.	Minneapolis
	Fleming, Dean S.	Minneapolis
	Fleming, Janice L.	St. Paul
	Fliehr, Richard R.	Minneapolis
	Flinn, James B.	Redwood Falls
	Floersch, Adrian J.	Owatonna
	Flom, Reynold P.	St. Paul
	Flom, Robert S.	St. Paul
	Flora, George C.	Minneapolis
	Florence, David W.	St. Paul
	Florine, Martin C.	Madison Lake
	Flory, William D.	Minneapolis
	Flynn, Bernard F.	Hibbing
	Flynn, Louis L., Jr.	St. Paul
	Foderick, John W.	Hastings
	Foderick, Peter P.	Ada
*	Fogelberg, Emil J.	St. Paul
	Foker, Leslie W.	Minneapolis
	Foley, Robert R.	Minneapolis
	Foley, William A.	Minneapolis
£	Folger, Walter N.	St. Paul
	Folsom, Louis B.	Minneapolis
	Foni, Iancu F.	Faribault
	Fontana, Robert S.	Rochester
	Forbes, Edward F.	Minneapolis
	Ford. William H.	Hopkins
£	Fordyce, Richard A.	Rochester
	Foreman, Richard T.	St. Paul
	Forsythe, James R.	St. Paul
	Fortier, George M. A.	Little Falls
	Fortier, George M. A., Jr.	Little Falls
	Fortier, Rene G.	Mankato
	Fortuny, Ignacio E.	Minneapolis
	Foss, Donald L.	Minneapolis
†	Foss, Edward L.	Condon, MT
§	Foster, Craig A.	Minneapolis
	Foster, Orley W.	Minneapolis
	Fox, Donald P.	St. Paul
	Fox, James Rogers	Minneapolis
	Fox, LeRoy J.	St. Paul
	Fraley, Elwin E.	Minneapolis
†	Franchere, Frederick W.	Lake Crystal
†	Francis, David W.	Morristown
	Frane, Donald B.	Minneapolis
	Frane, Gerald T.	Minneapolis
	Franklin, Gordon W.	Northome
£	Fraser, Richard A.	Rochester
†	Frederickson, Alice C.	Willmar
	Frederickson, David L.	Duluth
	Fredlund, Jon S.	Anoka
	Freeman, Charles D., Jr.	St. Paul
	Freeman, Craig W.	Minneapolis
	Freeman, Donald W.	St. Louis Park
	French, Bayard T.	Hibbing
	French, Lyle A.	Minneapolis
	Frerichs, Roger L.	Fergus Falls
£	Freshman, John R.	Rochester
	Frethem, Allen A.	Rochester
	Frey, Richard J.	Minneapolis
	Friberg, Joseph B.	Minneapolis
†	Fricke, Robert E.	Rochester
	Fried, Louis A.	Minneapolis
†	Friedell, Aaron	Minneapolis
	Friedell, George	Minneapolis
£	Friedell, Peter E.	Rochester
	Friedlieb, Oskar P.	Virginia
	Friedman, Harry S.	Minneapolis
	Friedrich, Bradford E.	Red Wing
	Friend, Charles A.	Minneapolis
†	Fritsche, Albert	New Ulm
	Fritsche, Carl J.	New Ulm
	Fritsche, Theodore R.	New Ulm
	Fritz, Wallace L.	St. Paul
£	Froehling, Rodney C.	St. Paul
	Fromke, Vincent L.	Minneapolis
	Frost, John B.	Minneapolis
	Frost, John W.	St. Paul
	Fruchtman, Stanley A.	Minneapolis
£	Fruen, Paul R.	St. Paul
	Frye, Charles W.	St. Paul
	Frys, Russell N.	Minneapolis
£	Frytak, Stephen	Rochester
#	Fuglestad, Edson V.	Minneapolis
	Fuglestad, J. Roald	Minnetonka
†	Fuller, Alice H.	Minneapolis
	Fuller, Benjamin F.	White Bear Lake
	Fuller, Josiah	Duluth
†	Funk, Victor K.	Hopkins
	Funke, Joyce L.	St. Paul
	Furlow, William L.	Rochester
	Furman, L. Christine	Minneapolis
	Furr, Leo	Bird Island
£	Fuster, Valentin	Rochester

G

	Gaard, Richard C.	Robbinsdale
	Gaebe, Milton B.	Clara City
	Gaertner, Frank M. J., Jr.	St. Paul
	Gaertner, John R.	St. Paul
	Gage, James R.	Minneapolis
	Gaida, Joseph B.	St. Cloud
	Gailitis, Veronika M.	St. Paul
	Gaither, Daniel W.	St. Paul
	Galbraith, Richard F.	Minneapolis
	Galejs, Aina	St. Paul
£	Gall, Randall J.	Rochester
	Gallagher, Larry J.	Mound
	Gallett, Lester E.	Minneapolis
	Galligan, John J.	St. Paul
†	Galligan, Margaret Mary D.	Minneapolis
	Galvin, Carroll	Sleepy Eye
	Galway, Charles F.	Minneapolis
†	Gambill, Carl M.	Rochester
†	Gambill, Earl E.	Rochester
	Gamble, Elbert J.	Roseville
	Gamble, William G.	Minneapolis
	Gamm, Edgar R.	Park Rapids
	Gannon, Paul G.	Minneapolis
	Garamella, Joseph J.	Minneapolis
	Garber, George L.	Winona
	Garber, James J.	Rochester
	Garcia. Oscar	Coon Rapids
£	Gard, Joseph R.	Rochester
	Gardner, Jack K.	Fairmont
	Gardner, Walter P.	St. Paul
	Garetz, Floyd K.	Minneapolis
*†	Garrow. Douglas M.	St. Paul
	Garske, George L.	Minneapolis
	Garten, Joseph L.	Minneapolis

	Garvey, James T.	Minneapolis
	Garvis, Gary E.	Minneapolis
	Gasik, Joseph M.	Minneapolis
	Gastineau, Clifford F.	Rochester
£	Gauger, David W.	Minneapolis
	Gault, N. L. Jr.	Minneapolis
	Gaute, Svend T.	St. Paul
	Gaviser, David	Minneapolis
	Gedgaudas, Eugene	Minneapolis
†	Gehlen, Joseph N.	St. Paul
	Geis, LeRoy F.	Minneapolis
	Geiser, Peter M.	Alexandria
	Geist, Robert W.	St. Paul
	Geller, Joseph	Minneapolis
	Gendron, Joseph L.	Minneapolis
	Gentry, William C., Jr.	Minneapolis
	George, Vane P., Jr.	LeSueur
	Geraci, Joseph E.	Rochester
	Gerend, Thomas J.	Virginia
	Gerstenkorn, George B.	Milaca
	Gerster, Paul W.	Anoka
	Gesundheit, Sim	Minneapolis
†	Geurs, Benjamin R.	Mankato
†	Ghostley, Mary C.	Bemidji
	Gibbs, Edward C.	St. Paul
	Gibbs, Robert W.	Minneapolis
	Giebenhain, John N.	Minneapolis
†	Giere, Joseph C.	Minneapolis
*†	Giere, Richard W.	Minneapolis
†	Giere, Silas W.	Benson
	Gilbert, Maurice G.	Minneapolis
	Gilbertsen, A. Sigrid	Minneapolis
	Gilbertsen, Victor A.	Minneapolis
	Gilbertson, David L.	St. Paul
£	Gilbertson, Gary F.	Bloomington
	Gilchrist, Milton R.	St. Paul
	Gill, Theodore M.	Albert Lea
	Gilles, Paul J.	Minneapolis
	Gilles, Thomas F.	Fairfax
	Gillespie, Delmar R.	St. Paul
†	Gillespie, Malcolm G.	Duluth
	Gillund, T. Dean	Minneapolis
	Gilman, Lloyd C.	Willmar
£	Gilsanz, Vicente	Rochester
	Gilsdorf, Donald A.	St. Paul
†	Gingold, Benjamin A.	Minneapolis
	Ginsberg, James P.	Minneapolis
	Gislason, Paul H.	Mankato
	Gisvold, John J.	Rochester
	Gjerde, William P.	Lake City
	Glaeser, John H.	Minneapolis
	Glass, David E.	Owatonna
	Glenny, William R.	St. Paul
	Glick, Dallas D.	Mountain Lake
£	Glista, Glen G.	Rochester
	Glomstad, Gary B.	Grand Rapids
	Godfrey, H. Wilson	Minneapolis
	Goehl, Reinhold O.	Minneapolis
	Goehrs, Gilman H.	St. Cloud
#	Goellner, John R.	APO San Francisco, CA
	Goetz, Frederick C.	Minneapolis
	Gokcen, Barbara W.	Minneapolis
	Gokcen, Muharrem	Minneapolis
†	Goldberg, Isadore M.	Minneapolis
	Goldberg, Marvin E.	Minneapolis
	Goldberg, Stanley M.	Minneapolis
	Goldfarb, Benjie L.	Minneapolis
	Goldfarb, Mace G.	Minneapolis
	Goldish, Daniel R.	Duluth
	Goldish, Robert J.	Duluth
†	Goldman, Theodore I.	Minneapolis
	Goldner, Meyer Z.	Minneapolis
	Goldschmidt, Volker	Duluth
	Goldsmith, Joseph W.	St. Paul
	Goldstein, Alan L.	Hopkins
	Goldstein, Norman P.	Rochester
	Goldston, Edgar C.	Rochester
£	Goldyne, Marc E.	Rochester
	Goltz, Robert W.	Minneapolis
	Gonzales, Neva M.	St. Cloud
	Good, C. Allen, Jr.	Rochester
	Good, Gary	Minneapolis
	Good, Roy H.	Faribault
	Goodchild, William R.	Minneapolis
	Goodale, Robert L., Jr.	Minneapolis
	Goodall, David C.	Deer River
	Goodman, Ernest	St. Paul
	Goodnow, William H.	Duluth
	Goott, Bernard	St. Paul
	Gorman, Jeffrey D.	Minneapolis
	Gorden, A. Marc	International Falls
	Gordon, John R.	Minneapolis
	Gordon, Sewell S.	Minneapolis
	Gorman, Colum A.	Rochester
	Gould, Allan B., Jr.	Rochester
#	Gould, Ronauld J.	Anchorage, AL
†	Govrik, Kalman	St. Paul
	Gowan, Lawrence R.	Duluth
	Gowan, Lawrence R., Jr.	Duluth
	Gower, Walter E.	Duluth
	Gozum, Ekrem	Minneapolis
	Grabow, Jack D.	Rochester
	Grados, Carlos	Coon Rapids
	Graf, John A.	Rochester
	Grage, Theodor B.	Minneapolis
	Graham, Asa B.	Faribault
	Graham, John J.	Minneapolis
	Graham, Richard O.	St. Paul
	Grahek, Jack P.	Ely
	Grande, David W.	Mankato
	Granger, Sylvia B.	St. Peter
	Grannis, Frederick W., Jr.	Rochester
	Granquist, Richard D.	Minneapolis
	Grant, James B.	Minneapolis
	Grant, John C.	Sauk Centre
	Grant, Suzanne	Minneapolis
	Gravett, Desmond C.	Rochester
†	Gray, Royal C.	Minneapolis
#	Greden, John F.	Ft. Lee, VA
	Green, Clayton R.	Excelsior
	Green, John F.	Alexander
	Green, Paul A.	Rochester
	Green, Robert A.	Minneapolis
	Greenberg, Albert J.	Minneapolis
	Greene, Gordon O.	Virginia
	Greene, Laurence F.	Rochester
	Greene, Leonard H.	Minneapolis
	Greenfield, Irving	Minneapolis
	Greenfield, Theodore	Champlin
	Gregoire, Earl	Bemidji
£	Greipp, Philip R.	Rochester
¶	Greisheimer, Esther M.	Philadelphia, PA
£	Grenier, Stephen R.	Minneapolis
	Gretsch, Gerald A.	St. Paul
	Grey, Mark A.	Waseca
#	Greydanus, Donald E.	Hawthorne, N.J.
	Gridley, John W.	St. Paul
	Griebie, Grant L.	Hutchinson

	Griffin, John W.	Bemidji
	Griffin, Patrick J.	St. Paul
	Griffin, Richard P.	Benson
	Grimes, Burton P.	St. Peter
	Grimes, Marian	Minneapolis
	Grimes, Paul T.	Park Rapids
	Grimm, Roger R.	Minneapolis
	Grimmell, Francis J.	Minneapolis
	Grinley, Andrew V.	Grand Rapids
†	Grinvalds, Anna O.	Cambridge
	Grohs, William H.	Duluth
	Gronquist, Y. K. J.	Cloquet
	Groover, Robert Vann	Rochester
	Grose, Frederick N.	Clarissa
	Gross, John B.	Rochester
	Grossling, Higinia	Minneapolis
	Grossling, Sergio	Minneapolis
	Groth, Mary K.	Detroit Lakes
	Grubbs, Larry T.	Rochester
	Grube, David W.	Minneapolis
	Gruys, Robert I.	Minneapolis
	Gudio, Felix A., Jr.	St. Paul
	Guerrero, Rafael A.	Minneapolis
	Guilfoile, Pierre J.	Delano
	Guiton, Carl R.	St. Paul
	Gullickson, Glenn, Jr.	Minneapolis
	Gumnit, Robert J.	St. Paul
	Gunlaugson, Frederick G.	Minneapolis
	Gustafson, Paul O.	Minneapolis
	Gustafson, Robert W.	Granite Falls
†	Gustason, Harold T.	Minneapolis
	Gustilo, Ramon B.	Minneapolis
	Gutenkauf, Jos. J.	Minneapolis
	Guthrie, J. Cameron	St. Paul
£	Guthrie, Richard B.	St. Paul
	Gutzmann, Bruce W.	Faribault
	Guy, Jack A.	New London
£	Gyory, Attila N.	Rochester

H

	Haas, Jack F.	Northfield
	Haas, John W.	Minneapolis
	Haase, Donald D.	Silver Bay
	Haavik, John E.	Duluth
£	Habein, Harold C.	Palo Alto, CA
	Haberle, Charles A.	Minneapolis
	Haddad, Nick J.	Minneapolis
	Haemmerle, James H.	St. Paul
†	Haes, Julius E.	St. Peter
	Haesly, Warren W.	Winona
	Hagberg, Norman L.	Montevideo
	Hagedorn, Albert B.	Rochester
	Hagen, John D.	Austin
	Hagen, Kristofer	Minneapolis
	Hagen, Wayne S.	Minneapolis
	Haglin, John J.	Minneapolis
	Hahn, Richard G.	Rochester
	Haight, James W.	St. Paul
†	Haines, Samuel F.	Rochester
	Hakanson, Erick Y.	St. Paul
	Hakim, Ali A.	Minneapolis
	Halbert, John J.	Duluth
†	Halenbeck, Philip L.	St. Cloud
	Hall, Arthur M.	Minneapolis
	Hall, Barnard	St. Paul
	Hall, Frederick C.	Minneapolis
	Hall, Harry B.	Minneapolis
	Hall, Loren J.	Minneapolis
	Hall, Wendell H.	Minneapolis
†	Hallberg, Olav Erik	Rochester
	Hallgren, Roger	Belle Plain
	Halliday, Phillip V.	Duluth
	Hallin, Roger P.	Worthington
†	Halloran, Walter H.	Jackson
	Halme, William B.	Wadena
	Halper, Bernard	Hibbing
£	Halpin, John A.	Rochester
	Halverson, D. E.	Highland, CA
	Halverson, Kermit J.	Parkville
	Halverson, William G.	Madelia
	Halvorsen, Daniel K.	Owatonna
#	Halvorsen, John G.	Clinton
	Halvorson, David C.	Northfield
	Halvorson, Harold C.	Albert Lea
	Halvorson, James W.	Zumbrota
	Hambidge, Gove, Jr.	Minneapolis
	Hamel, Arnold L.	Minneapolis
	Hamel, Joseph I.	Minneapolis
	Hammar, Lawrence M.	Mankato
	Hammerstrom, Robert N.	Minneapolis
	Hammes, Ernest M., Jr.	St. Paul
£	Hancock, William E.	Rochester
	Handler, Seymour	Minneapolis
	Hanisch, Edward C., Jr.	Minneapolis
	Hankerson, Robert G.	Mankato
	Hanlon, David G.	Rochester
	Hannon, Donald W.	St. Paul
†	Hansen, Cyrus O.	Minneapolis
	Hansen, Milo L.	Little Falls
†	Hansen, Olga S.	Minneapolis
	Hansen, Robert E.	Hibbing
	Hansen, Rollin M.	Minneapolis
	Hansen, Theodore M.	Albert Lea
	Hanske, Edward A.	Minneapolis
	Hanson, A. Stuart	Minneapolis
£	Hanson, Ernest J., Jr.	Rochester
	Hanson, Ernest O.	Cloquet
†	Hanson, Everett	New York Mills
†	Hanson, Harlow J.	Minneapolis
	Hanson, Harold B.	Burnsville
	Hanson, Harold W.	Minneapolis
	Hanson, Lewis	Frost
	Hanson, Mark C. L.	Minneapolis
	Hanson, Mildred S.	Minneapolis
	Hanson, Norbert O.	Rochester
	Hanson, Norman P.	Rochester
	Hanson, Stephen L.	Minneapolis
*†	Hanson, William A. H.	Minnetonka
	Hanson, William B.	Minneapolis
	Hanton, Edward M.	St. Paul
	Harbaugh, John T.	St. Cloud
†	Hargraves, Malcolm M.	Rochester
	Harkness, John W.	Minneapolis
	Harmon, Gaius E.	St. Paul
£	Harper, David G.	Duluth
	Harrington, Vernon A.	Duluth
	Harris, Boyd L.	St. Paul
£	Harris, James D.	Minneapolis
	Harris, John E.	Minneapolis

	Harris, Leon D.	Minneapolis
	Harris, Max E.	St. Paul
	Harrison, Percy W.	Worthington
†	Harrison, William C.	Minneapolis
	Hart, Terril H.	Wayzata
†	Hart, William E.	Monticello
†	Hartfiel, William F.	St. Paul
	Hartfield, James E., Jr.	Rochester
	Hartig, Marjorie	St. Paul
	Hartig, Paul R.	Minneapolis
	Hartman, Evelyn E.	Minneapolis
	Hartman, Glen W.	Rochester
	Hartman, Gene R.	Minneapolis
	Hartmann, Ronald J.	Rochester
	Hartnagel, Grant F.	Red Wing
	Hartung, Elmer H.	Claremont
	Hartwich, Roger F.	Winona
	Hartwig, John A.	Minneapolis
	Harty, Jerome L.	Minneapolis
	Hartzler, Geoffrey O.	Minneapolis
	Hartzler, Paul L.	Cambridge
	Harvey, Clyde B.	Minneapolis
	Hass, Frederick M.	Minneapolis
	Hastings, Donald W.	Minneapolis
	Hauff, Karen J.	Rochester
	Hauge, Erling T.	Minneapolis
†	Hauge, Malvin I.	Marcell
	Haugen, George W.	Minneapolis
	Haugen, John A.	Minneapolis
	Haus, Erhard	St. Paul
	Hauser, Charles W.	St. Paul
	Hauser, Donald C.	Minneapolis
†	Hauser, Victor P.	St. Paul
	Hauser, W. Allen	St. Paul
	Hausman, William	Minneapolis
	Havel, Robert J.	Minneapolis
	Haven, Walter K.	Minneapolis
	Havig, Terrance A.	Lexington, KY
	Hawk, Dale J.	Rochester
	Hawkinson, Harlan W.	St. Paul
†	Hawkinson, Raymond P.	Minneapolis
	Hawley, George M. B., II	Red Wing
	Hay, Lyle J.	Minneapolis
	Hayashi, Melvin M. K. W.	Belleville, IL
	Hayes, Albert F.	St. Paul
	Hayles, Alvin B.	Rochester
	Haywa, E. William	Minneapolis
	Hazen, Richard W.	Willmar
	Heagle, C. Russell	Waconia
	Hebbel, Robert	Minneapolis
†	Hebeisen, Milton B.	Chaska
†	Heck, Frank J.	Rochester
†	Heck, William W.	St. Paul
	Hedemark, Homer H.	Ortonville
†	Hedemark, Truman A.	Ortonville
	Hedenstrom, Charles W.	St. Paul
†	Hedenstrom, Frank G.	St. Paul
	Hedenstrom, Philip C.	Marshall
	Hedenstrom, Richard H.	St. Paul
	Hedrick, William L.	Minneapolis
	Heegaard, William G.	Alexandria
	Hegrenes, Robert L.	Hutchinson
	Hegstad, Thomas C.	Windom
†	Heiam, William C.	Cook
	Heiberg, Olaf M.	Worthington
	Heid, James K.	Little Falls
	Heidel, Werner	Rochester
	Heimel, Albert J.	St. Paul
	Heinz, Ivy B.	Shakopee
	Heinz, John N.	Minneapolis
	Heinzerling, Carl R.	Chaska
	Heise, Carl vR	Winona
	Heise, Herbert vR	Winona
	Heise, Paul vR	Winona
	Heise, Phillip vR.	Winona
	Heise, William vR	Winona
	Heisel, John G.	Duluth
£	Heiss, Frederick W.	Rochester
#	Heithoff, Kenneth B.	Bloomington
	Held, William J.	St. Cloud
	Helgaas, Steffen A.	Farmington
	Heller, Ben I.	Minneapolis
	Heller, Edgar E.	Mankato
£	Heller, Stephen F.	Rochester
	Heller, Steven A.	Minneapolis
	Helmholz, Henry F., Jr.	Rochester
†	Helseth, Hovald K.	Fergus Falls
	Helseth, Hovald K. Jr.	Minneapolis
	Helwig, Karl L.	Virginia
	Hempel, Dean J.	Minneapolis
	Henderson, Edward D.	Rochester
	Hendrickson, John M.	St. Paul
	Henderson, John W.	Rochester
	Henderson, Lowell L.	Rochester
	Henderson, Terrance P.	White Bear Lake
	Hengel, James A.	St. Paul
†	Hengstler, William H.	St. Paul
	Henke, Clarence E.	St. Paul
	Henke, Wilbert J.	St. Paul
	Henrickson, Ronald R.	Rochester
	Henrikson, Earl C.	Minneapolis
†	Henry, Clarence J.	Onamia
	Henry, James S.	St. Paul
	Henry, John C.	Owatonna
	Henry, Joseph E.	Milaca
	Henry, Kenneth G.	Owatonna
	Henry, Stephen	Osakis
	Henwood, Wesley C.	Virginia
	Hepper, Norman G.	Rochester
	Herber, Leo	Thief River Falls
†	Herbert, Willis L.	Minneapolis
	Hergott, Patrick F.	Waseca
	Herland, Alexander L.	Winona
†	Herman, Samuel M.	Fort Lauderdale, FL
	Hermans, Paul E.	Rochester
	Hernandez, Hermenegildo, Jr.	Minneapolis
	Herrell, Wallace	Rochester
	Herrick, Donald W.	St. Paul
†	Hertel, Garfield E.	McAllen, TX
	Hesla, Inman A.	Austin
	Hess, Carroll N.	Minneapolis
	Hess, Sheldon T.	Minneapolis
	Hetzler, John A.	Minnetonka
§	Heuer, Marvin A.	Inver Grove Heights
	Heupel, Hermann W.	Minneapolis
†	Hewitt, Edith S.	Rochester
	Hewitt, Marshall I.	Minneapolis
	Hiatt, John A.	Minneapolis
	Hickok, David F.	Minneapolis
	Hiduchenko, Katherine	Minneapolis
	Hildebrand, John E.	Bemidji
	Hildebrandt, Walter C.	Minneapolis
†	Hilding, Anderson C.	Duluth
	Hilgedick, William R.	Minneapolis
	Hilger, Jerome A.	St. Paul
	Hilger, Laurence D.	St. Paul
	Hilgers, Robert D.	St. Paul

	Hilgermann, George O.	Minneapolis
	Hilker, Marcus D.	St. Paul
	Hilker, Robert T.	Owatonna
	Hill, Charlotte W.	St. Paul
	Hill, Daniel E.	St. Paul
	Hill, David L.	Minneapolis
	Hill, Earl	Minneapolis
	Hill, Elmer M.	Minneapolis
£	Hill, John J.	Minneapolis
	Hill, John R.	Rochester
	Hill, Richard W.	Rochester
	Hiller, Bruce H.	Minneapolis
	Hinckley, Robert G.	White Bear Lake
	Hinderaker, Harris P.	Willmar
	Hines, Edgar A., Jr.	Brevard, NC
†	Hiniker, Louis P.	St. Paul
†	Hiniker, Peter J.	St. Peter
	Hinz, Walter E.	Willmar
	Hippchen, Ray C.	St. Paul
£	Hirsch, Blayne L.	Rochester
	Hirsh, Stanton A.	Crookston
	Hitchcock, Claude R.	Minneapolis
	Hoagland, H. Clark	Rochester
	Hobday, H. Thomas	St. Cloud
	Hodapp, Robert V.	Willmar
	Hodges, Kenneth V.	Minneapolis
¶	Hodgin, Carol L.	Rochester
	Hodgson, Corrin H.	St. Paul
£	Hodgson, Corrin J.	Rochester
	Hodgson, Jane E.	St. Paul
	Hodgson, John R.	Rochester
	Hoeg, Dwight C.	Duluth
	Hoekstra, Ronald	Minneapolis
†	Hoeper, Philip G.	Chestnut Hill, MA
	Hoff, Herbert O.	Duluth
†	Hoffert, Henry E.	Minneapolis
	Hoffman, David L.	Rochester
	Hoffman, Neil R.	Minneapolis
†	Hoffman, Roy A.	Minneapolis
	Hoffman, Walter Lees	Minneapolis
	Hofmann, Gerald N.	Minneapolis
	Hohmann, Albert	St. Paul
	Holbrook, Margaret A.	Rochester
†	Holcomb, Gerald R.	Rochester
†	Holcomb, Joel T.	Marine-on-the-St. Croix
	Holland, C. R.	Rochester
	Hollenhorst, Robert W.	Rochester
	Hollinshead, W. H.	St. Paul
	Holm, Donald F.	Minneapolis
	Holm, Owen W.	Hibbing
	Holman, Colin B.	Rochester
	Holmberg, Conrad J.	Minneapolis
	Holmen, Douglas J.	St. Paul
	Holmes, H. Spencer	Minneapolis
	Holmstrom, Carle H.	Warren
	Holstine, John D.	Fairmont
	Holt, Douglas J.	Minneapolis
	Holt, Glen E.	Duluth
†	Holt, John E.	St. Paul
	Holten, John R.	Moorhead
	Holzapfel, Fred C.	Minneapolis
	Hom, Leong Y. W.	Fergus Falls
	Honath, Donald H.	Owatonna
	Hood, Roderick P.	Duluth
	Hopkins, G. Wendell	Minneapolis
	Hopperstad, J. Jerome	Minneapolis
	Hoppes, Emerson E.	Minneapolis
	Horecki, Henry	Minneapolis
	Horn, Allen	Melrose
	Horns, Howard L.	Minneapolis
	Horns, Norman	Minneapolis
	Horns, Richard C.	Minneapolis
	Horowitz, Arthur J.	Minneapolis
	Horowitz, Mancel I.	Minneapolis
	Hostetter, James P.	Minneapolis
†	Horton, Bayard T.	Rochester
	Hoseth, Wayne L.	Minneapolis
	Hosfield, William B.	Minneapolis
	Hottinger, George C.	St. Paul
	Hottinger, Raymond C.	Janesville
	Houglum, Arvid J.	Duluth
†	Houkom, Bjarne	Fergus Falls
†	Houkom, S. Sverre	Duluth
	Houle, Rollin J.	New Brighton
	Houlton, William H.	St. Paul
	House, James H.	Minneapolis
	House, Roy F., Jr.	Minneapolis
	Householder, James R.	Minneapolis
	Houser, Otis	Rochester
	Houts, Joseph C.	Dassel
	Hovde, Gordon W.	Lindstrom
	Hover, James R.	Aitkin
†	Hovland, Melvin L.	Minneapolis
	Hovland, Richard D.	Minneapolis
	Howard, David	Long Prairie
	Howard, Frank M., Jr.	Rochester
#	Howard, Malin L.	St. Paul
£	Howard, Richard J.	Edina
	Howard, Robert B.	Minneapolis
	Howard, Solomon E.	Minneapolis
	Howe, Newell W.	West St. Paul
	Howell, Carter W.	Minneapolis
	Howell, John L.	Minneapolis
	Howell, Llewelyn P.	Rochester
	Hoyt, C. Sherman	Minneapolis
	Hruza, William J.	Sioux Falls, SD
	Huang, Ta Yu	Waconia
£	Hu, Chung-Hong	Rochester
	Huber, Robert W.	St. Croix Falls, WI
*	Hubin, Edwin G.	Sandstone
	Huebert, Dan W.	Hutchinson
£	Huerta, Enrique	Rochester
	Huff, John S.	Minneapolis
	Huffington, Herb L.	Waterville
†	Huffington, Herbert L.	Lutsen
	Hughes, Bernard J.	St. Cloud
	Hughes, Sidney O.	Winona
	Hulteng, Donald B.	Minneapolis
	Hunder, Gene G.	Rochester
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	Hunt, James C.	Rochester
	Hunt, Kai K.	Alexandria
¶	Hunt, Max L.	Rochester
	Hunt, Vincent R.	Minneapolis
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	Hung, Jui-Sung	Minneapolis
	Hunter, Murray H.	Farmington
	Hunter, Samuel W.	St. Paul
	Hurr, Maland C.	Minneapolis
	Hurwitz, Milton M.	St. Paul
	Huseby, Thomas L.	St. Paul
	Husebye, Kjeld O.	St. Paul
	Hustad, Edward G.	Minneapolis
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	Hymes, Alan C.	Minneapolis
†	Hymes, Charles	Minneapolis
#	Hynes, Kieran M.	Wright-Patterson AFB, OH

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	Ide, Arthur W., Jr.	Minneapolis
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	Ingalls, Edgar G.	Minneapolis
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	Isele, Reginald H.	Austin
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	Iverson, Eleanor B.	Minneapolis
	Iverson, Jerry A.	St. Cloud
£	Iverson, Paul C.	Minneapolis
	Iverson, Rolf M.	Minneapolis
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	Jacklin, Alexander J.	Duluth
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	Jacobson, Leslie W.	Minneapolis
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	Jacobson, Wyman E.	Minneapolis
	Jacoby, John S.	Minneapolis
	Jacott, William E.	Duluth
	Jaeger, Dwight E.	St. Cloud
	Jaffe, Manuel O.	Minneapolis
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§	James, Ellery M. Jr.	St. Paul
	James, John W.	St. Paul
	Janda, George W.	Minneapolis
	Janecek, James, Jr.	St. Paul
	Janecky, Allen G.	Baudette
	Janes, Alec L.	Minneapolis
	Janes, Joseph M.	Rochester
	Janssen, Martin E.	St. Paul
	Jantunen, Kaucho I.	New York Mills
	Jarvis, Charles W.	St. Paul
	Jastram, Rupert M.	St. Paul
	Jay, Alan R.	Temple, TX
	Jefferies, William L.	Minneapolis
	Jensen, Alvin M.	Brownton
	Jensen, James E.	Stillwater
	Jensen, John A.	Crookston
	Jensen, Nathan K.	Minneapolis
	Jensen, Paul A.	Minneapolis
	Jensen, Reynold A.	Minneapolis
	Jensen, James E.	Stillwater
	Jerome, Bourne	Minneapolis
	Jerome, Elizabeth B. K.	Minneapolis
	Jeronimus, Henry J.	Duluth
	Jeub, Robert P.	Minneapolis
£	Jibilian, Artin Y.	Rochester
	Jimenez, Edward	Duluth
	Jo, Wenancio T.	Minneapolis
	Johanson, James E.	Minneapolis
	John, Byron L.	St. Cloud
	Johnson, Alan R.	Minneapolis
	Johnson, Aldridge F.	St. Paul
	Johnson, Angelo G.	Minneapolis
	Johnson, Arthur B.	Minneapolis
	Johnson, Bradley D.	Minneapolis
	Johnson, Byron P.	St. Paul
	Johnson, Calvin J.	Grand Rapids
	Johnson, Carl Edwin	St. Paul
	Johnson, Carl Eric	Rochester
	Johnson, Carolyn A.	St. Paul
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	Johnson, Curtis M.	Winona
	Johnson, Daniel A.	Litchfield
	Johnson, Daniel T.	St. Paul
	Johnson, David R.	Minneapolis
£	Johnson, David W.	St. Paul
#	Johnson, Donald A.	Minneapolis
	Johnson, Douglas L.	Brainerd
	Johnson, Edward A.	Minneapolis
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	Johnson, Einer W., Jr.	Rochester
	Johnson, Frank E.	Minneapolis
	Johnson, Franklin L.	Duluth
	Johnson, Frederick W.	Minneapolis
	Johnson, Gordon E.	Minneapolis
	Johnson, Harry A., Jr.	Minneapolis
	Johnson, Herbert W.	St. Paul
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	Johnson, Lyle O.	St. Paul
	Johnson, Mark H.	Minneapolis
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	Johnson, Norman Paul	St. Paul
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	Johnson, Paul E.	Wayzata
	Johnson, Phillip S.	Minneapolis
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	Johnson, Reinald G.	Minneapolis
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	Johnson, Richard J.	St. Paul
	Johnson, Richard S.	Minneapolis
	Johnson, Richard V.	Minneapolis
	Johnson, Robert E.	Minneapolis
	Johnson, Robert H.	St. Paul
	Johnson, Roger A.	St. Paul
	Johnson, Roger L.	St. Paul
	Johnson Stanley M.	White Bear Lake
	Johnson, Theodore L.	Duluth
	Johnson, Thomas E.	St. Paul
	Johnson, Thomas H., Jr.	Minneapolis
	Johnson, Vilhelm M.	Dawson
	Johnson, William E.	St. Cloud
	Johnson, William J.	Rochester
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	Johnston, H. Wayne	Virginia
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	Jones, Richard H.	Minneapolis
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	Jones, Thomas K. Jr.	Minneapolis
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	Jordan, Robert E.	Rochester
	Jorgensen, Edward O.	Rochester
	Jorgensen, Donald R.	Willmar
	Jorgensen, Harlan	Minneapolis
	Joseph, Arnold H.	St. Paul
	Joyce, John W.	Rochester
	Judd, Allen S.	Minneapolis
	Judd, Edward S.	Rochester
†	Judd, Walter H.	Washington, D.C.
†	Juergens, Herman M.	Belle Plaine
	Juers, Edward H.	Red Wing
	Juntunen, Roy R.	Duluth
†	Jurdy, Mitchell	Minneapolis
†	Just, Herman J.	Hastings

K

	Kaczrowski, William M.	Marshall
	Kadesky, Harold B.	Minneapolis
	Kaese, Werner E.	Rochester
#	Kaine, Richard F.	St. Albans, NY
	Kaiser, Harold B.	Minneapolis
	Kaiser, Milton L.	New Ulm
	Kalb, Thomas J.	Minneapolis
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	Kaminski, Gregory W.	Redwood Falls
	Kampen, Charles D.	Grand Rapids
	Kane, Dennis J.	Minneapolis
	Kane, Morton C.	Minneapolis
	Kane, William J.	Chicago. IL
	Kanne, Earl R.	Brainerd
#	Kantack, Paul W.	Keesler, MS
	Kantar, Yale C.	St. Paul
	Kaplan, Arnold P.	Minneapolis
	Kaplan, David H.	Edina
*	Kaplan, J. Jacob	Minneapolis
	Kaplan, Martin B.	Minneapolis
	Kapps, F. Donald	St. Paul
	Karan, E. K.	Albert Lea
	Karges, Laurel E.	Grand Rapids
	Karish, Louis J.	Grand Rapids
	Karleen, Conrad I.	Minneapolis
	Karlen, Markle	Minneapolis
£	Karlowski, Thomas R.	Rochester
	Karn, Jacob F.	Ortonville
	Karnes, William E.	Rochester
£	Karrow, John W.	Rochester
	Karon, Everett H.	St. Paul
	Karon, Irvine M.	St. Paul
#	Karsebm, Frab S.	Clinton
†	Kasper, Eugene M.	St. Paul
	Kasper, Robert E.	Minneapolis
	Kassulke, Jan T.	Shakopee
†	Kath, Reinhard H.	Merrifield
	Katkov, Harold	Minneapolis
	Katz, Beni	Minneapolis
	Katz, Harry I.	Minneapolis
†	Katz, Louis J.	Long Beach, CA
	Kaufman, Edward J.	Appleton
	Kaye, Dale R.	Minneapolis
	Kazmier, Francis J.	Rochester
	Kearns, Thomas P.	Rochester
	Keenan, Thomas P.	St. Paul
	Kegel, James F.	Minneapolis
	Keil, Marcus A.	Albert Lea
†	Keith, Haddow M.	Rochester
†	Keith, Norman M.	Rochester
	Keith, Paul J.	Milaca
	Keithahn, Elmer E.	Sleepy Eye
	Keithahn, Mearl M. K.	Lamberton
	Kelalis, Panayotis P.	Rochester
†	Kelby, Gjert M.	Minneapolis
	Keldahl, Loren R.	Minneapolis
	Keller, Curtis	White Bear Lake
	Kelley, Roger E.	Crosby
	Kelly, Charles F.	Minneapolis
	Kelly, Edward H.	St. Paul
	Kelly, Helen M.	West St. Paul
	Kelly, James H.	St. Cloud
	Kelly, John C.	Minneapolis
	Kelly, John F.	Cold Spring
	Kelly, John P.	Minneapolis
	Kelly, John T.	Minneapolis
	Kelly, Joseph R.	St. Paul
	Kelly, Patrick J.	Rochester
	Kelly, Robert T.	Grand Rapids
	Kelly, William D.	Minneapolis
£	Kelman, Donald B.	Rochester
†	Kelsey, Carleton G.	St. Paul
	Kelsey, Chauncey M.	St. Paul
†	Kemp, Alphonse F.	Mankato
£	Kemp, Fred V.	Hopkins
	Kennedy, Byrl J.	Minneapolis
	Kennedy, Charles C.	Rochester
*	Kennedy, Claude C.	Minneapolis
†	Kennedy, George L.	Faribault
	Kennel, Arthur J.	Rochester
	Kenyon, Thomas J.	St. Paul
†	Kernohan, James W.	Rochester
	Kerr, Frederick W. L.	Rochester
†	Kesting, Herman	St. Paul
	Ketola, Launo E.	Glencoe
	Kevern, Jay L.	Henning
£	Key, Samuel N., III	San Francisco, CA
	Keyes, Robert W.	Pipestone
	Keys, Thomas F.	Rochester
	Khorsand, Darius	Minneapolis
	Kieffer, Stephen A.	Minneapolis
	Kiely, Joseph M.	Rochester
	Kierland, Robert R.	Rochester
	Kiernan. John H.	St. Paul
	Kiesler, Frank	Grand Rapids
†	Kilbride, Edwin A.	Worthington
§	Kile, Robert M.	Winona
	Kilen, Mark B.	Duluth
	Kim, Hyun-Houk	San Antonio, TX
	Kim, Kyoung	Worthington
	Kim, Mark K.	St. Paul
	Kim, Suck Wong	Minneapolis
	Kimmel, George E.	Rochester

	Kincaid, Owings W.	Rochester
	Kind, Allan C.	Minneapolis
†	King, Frances W.	Minnetonka
	Kinkade, Byron R.	Ada
	Kinney, William N.	Anoka
	Kiolbasa, Edward B.	Stillwater
†	Kippen, Neil	Breckenridge
	Kirby, Thomas J., Jr.	Rochester
	Kirklin, John W.	Birmingham, AL
	Kiser, Joseph C.	Minneapolis
£	Kishel, Gene F.	Rochester
	Kitzberger, Peter J.	New Ulm
	Kjellsen, Douglas L.	Minneapolis
	Kjellstrand, Carl M.	Minneapolis
	Klass, Donald W.	Rochester
	Klassen, Arthur C.	Minneapolis
	Klefstad, Lloyd H.	Greenbush
†	Klein, Harry	Duluth
	Kleinkauf, Thomas P.	Hutchinson
	Kleinsasser, Warren L.	St. Paul
	Kleven, Lowell H.	Minneapolis
	Kluge, John W.	St. Paul
	Knabe, George W.	Duluth
	Knapp, James F.	Detroit Lakes
	Knapp, Miland E.	Minneapolis
†	Knight, Ralph T.	Minneapolis
†	Knight, Ray R.	Minneapolis
	Knip, Robert J.	Ortonville
	Knipp, William J.	Brainerd
	Knobloch, William H.	Minneapolis
	Knoche, Harvey A.	Gaylord
	Knoedler, John P.	Duluth
†	Knoll, W. V.	Brainerd
	Knott, John W.	Forest Lake
	Knowles, Richard A.	Coon Rapids
	Knowles, Roy C.	St. Paul
	Knowles, William D.	Mankato
	Knudsen, Helen L.	Minneapolis
	Knutson, Gerhard E.	St. Paul
	Knutson, Lewis A.	Spring Grove
	Knutson, Robert C.	St. Paul
	Kodres, Nina	St. Paul
	Koelz, Thomas A.	St. Paul
	Koenig, Robert P.	St. Cloud
*	Kohlhase, Robert E.	Minneapolis
	Kohlmeyer, Albert	Fergus Falls
	Kohls, Gary G.	Milaca
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	Kolars, Charles P.	Minneapolis
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†	Koller, Hermann M.	Minneapolis
	Koller, Robert L.	Minneapolis
	Kolp, Berton A.	Glenwood
	Konicek, Robert G.	Rochester
	Kooda, Jennings C.	Morris
	Koontz, Peter S.	Minneapolis
	Koop, Severin H., Jr.	St. Cloud
	Koos, Gerald W.	Minneapolis
	Korchik, John P.	Minneapolis
	Korda, Henry A.	Pelican Rapids
	Koropchak, Nikolai	Minneapolis
¶	Kortz, Louise S.	Rochester
	Kostick, Joseph	Rochester
	Kosiak, Michael	St. Paul
	Kosiak, William	St. Paul
	Kostich, Nikola D.	Minneapolis
¶	Kostick, Joseph	Rochester
†	Kostick, William R.	Fertile
†	Kotchevar, Frank R.	Sun City, CA
	Kottke, Frederic J.	Minneapolis
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	Kotval, Russell J.	Pipestone
†	Koucky, Rudolph W.	Sagle, ID
	Kovack, Freeman D.	Minneapolis
	Kovacs, J. Curtis	St. Paul
	Koza, Donald W.	St. Paul
	Kozak, Michael J.	Minneapolis
	Kozel, William J.	Morris
	Kraemer, George N.	Fairmont
	Krafft, Walter E.	Minneapolis
	Kragh, Lyle V.	Minneapolis
	Kramer, Daniel W.	Minneapolis
	Kramer, James D.	St. Paul
	Krasnow, Brian M.	Minneapolis
	Krause, Carl W.	Fairmont
	Kreiser, Robert D.	Fergus Falls
	Kremen, Arnold J.	Minneapolis
	Kremer, Jerome L.	Montevideo
†	Kreuzer, Titus C.	New Brighton
	Krezowski, Thomas K.	St. Paul
	Kriel, Robert L.	St. Paul
	Krieser, Albert E.	Minneapolis
£	Krohn, John R.	Rochester
	Kronenberg, Richard S.	Minneapolis
	Krueger, Bruce R.	Rochester
	Kruger, E. Larry	Hallock
	Krupp, Neal E.	Rochester
	Kruzich, Stephen J.	St. Cloud
	Krystosek, Lee A.	Minneapolis
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	Kucera, Stanley T.	Northfield
†	Kucera, William J.	Santa Barbara, CA
	Kuehner, Marvin E.	Red Wing
§	Kuettner, John F.	Minneapolis
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	Kuhlmann, Lawrence B.	Melrose
	Kuhlmann, Vernon G.	Alexandria
	Kulstad, Oscar S.	Dodge Center
	Kump, Warren L.	Minneapolis
	Kundel, Donald W.	Duluth
	Kuske, Albert W.	St. Paul
	Kuslich, Stephen	Burnsville
	Kusske, Bradley W.	St. Paul
	Kusske, Douglas R.	St. Paul
	Kussy, James C.	Little Falls
	Kusz, Clarence V.	Minneapolis
	Kuz, Eugene L.	Savage
	Kvam, Lowell L.	St. Paul
	Kvamme, Brynjulv	Mabel
	Kvistberg, Gerald K.	St. Cloud
	Kwako, Jerome E.	Duluth
	Kyle, Robert A.	Rochester
	Kyllo, John E.	Minneapolis
	Kyllonen, Ronald R.	Edina

L

L'Abbe, A. J. Philip	Duluth
L'Heureux, Philippe R.	Minneapolis
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Labayen, Ricardo A	Waconia

	Labrecque, Pierre-Georges	Rochester
	LaBree, John W.	Minneapolis
	LaBree, Robert H.	Duluth
	Lackore, Leonard K.	Willmar
	Lade, Roswith I.	St. Paul
	LaFave, James W.	St. Paul
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	Lagaard, Sheldon	Minneapolis
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	Lamb, H. Douglas	Chattahoochie, FL
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	Lampert, Ronald M.	St. Paul
	Lamusga, David J.	Minnetonka
	Landsman, Gordon S.	Minneapolis
	Lane, Jerald P.	Minneapolis
	Lane, Miles I.	White Bear Lake
	Lang, Leonard A.	Minneapolis
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	Lannin, Donald R.	St. Paul
	Lannon, James B.	Minneapolis
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	Larsen, Frank W.	Minneapolis
£	Larsen, Russell H.	Minneapolis
	Larson, Allen K.	Minneapolis
	Larson, Arthur K.	Minneapolis
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	Larson, Donald Marvin	Duluth
	Larson, Donald Myren	Minneapolis
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	Larson, Dorette W.	Fergus Falls
	Larson, Ernest J., Jr.	Minneapolis
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	Larson, F. Wilmer	Minneapolis
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	Larson, Keith D.	Minneapolis
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	Larson, Paul H.	Minneapolis
	Larson, Richard E.	Minneapolis
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	Larson, Theodore G.	Brainerd
	Larson, Wyllis G.	Minneapolis
	Larter, Roland R.	Hallock
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	Lavender, Dick R.	St. Louis Park
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	Lawler, Kevin M.	St. Paul
	Lawrence, Van S.	Minneapolis
	Lawrow, John W.	Minneapolis
	Laws, Edward R., Jr.	Rochester
	Lawson, Warren R.	Minneapolis
	Lawton, James J., Jr.	Minneapolis
	Laxdal, Stefan D.	Minneapolis
	Layer, James M.	Minneapolis
	Layman, Thomas E.	St. Paul
	Layton, Donald D. Jr.	Rochester
	Leach, Clifford G.	St. Paul
	Leach, Thomas C.	Hudson, WI
	Leaf, Donn	Red Wing
	Leahy, Dennis M.	St. Paul
	Leary, Frank J.	Rochester
	Leavenworth, Richard O., Jr.	Minneapolis
†	Leck, Paul C.	Palm Desert, CA
	Lee, Gordon E.	Glenwood
*†	Lee, Hubert W.	Brainerd
	Lee, Ju Hao	Minneapolis
	Lee, Myoung Chong	Minneapolis
	Lee, Norman J.	Tracy
	Lee, Raymond A.	Rochester
	Lee, Robert E.	Rochester
	Lee, William C.	Hibbing
	Leek, Joseph H.	Duluth
	Leemhuis, Andrew J.	Minneapolis
	Lees, David C.	Minneapolis
	Lees, Jack R.	St. Paul
	Lehman, Donald S.	St. Paul
	Lehmann, James D.	Waconia
	Lehrer, Alfred J., Jr.	Montgomery
	Leick, Richard M.	St. Paul
	Leider, Lloyd L.	St. Paul
	Leiferman, Robert J.	Minneapolis
	Leighton, John S.	Minneapolis
	Leino, Walter B., Jr.	Ely
	Leinonen, Wendla E.	Anoka
£	Leist, Frederick D.	Rochester
†	Leitch, Archibald	South St. Paul
	Leitch, Cecil	Litchfield
	Lelwica, Thaddeus J.	Staples
†	Lenander, Mellvin E. L.	St. Peter
	Lenarz, Albert J.	St. Cloud
	Lenz, Bernard W.	Minneapolis
	Lenz, Joseph R.	Morton
	Lenz, Otto	Minneapolis
	Leonard, Paul F.	Rochester
	Leonard, Samuel	Minneapolis
	Leonard, Stanley A.	St. Paul
	Leonardson, Peter Y.	Silver Bay
	Leppo, N. Erkki A.	Duluth
	Lerdahl, Kenneth	St. Paul
	Lerner, A. Ross	Minneapolis
	Lerner, Irving J.	St. Paul
	Lerud, M. Mark	Detroit Lakes
	Leslie, Loren R.	Minneapolis
	Leslie, W. Robert	Minneapolis
	Lessard, Richard J.	St. Paul
	Lester, John W.	Mapleton
	Lester, Malcolm J., Jr.	Truman
	Lester, Theodore H.	Minneapolis
	Letson, Robert D.	Minneapolis
†	Leven, N. Logan	St. Paul
	Leverenz, Carleton W.	St. Paul
	Levine, Howard M.	Minneapolis
	Levine, Norman D.	Minneapolis
	Levitan, Leonard H.	St. Paul
	Levitt, George X.	St. Paul
	Levitt, Seymour H.	Minneapolis
†	Levy, Michael	Minneapolis
#	Levy, Jonathan M.	Albuquerque, NM
	Lewis, Charles W.	Henning

	Lewis, F. Bruce	Minneapolis
	Lewis, Glenn M., Jr.	Minneapolis
	Lewis, Joyce S., Jr.	Minneapolis
	Lick Louis C.	Minneapolis
	Lick, William J.	St. Paul
	Liebhaber, Henia F.	Anoka
	Lien, Richard J.	St. Paul
†	Lightbourn, Edgar L.	Hastings
	Lilleberg, Norbert J.	St. Paul
	Lillehei, James P.	Minneapolis
	Lillehei, Richard C.	Minneapolis
	Lillemoen, Roger D.	Minneapolis
	Lillie, Andrew R.	St. Paul
	Lillie, John C.	Rochester
	Lima, Ludvig R.	Montevideo
	Limbeck, Donald A.	Minneapolis
	Lindahl, Merlyn J.	Sherburn
	Lindall, Arnold W., Jr.	Minneapolis
	Lindberg, Evan F.	Minneapolis
	Lindberg, Vernon L.	Minneapolis
	Lindberg, Winston R.	Minneapolis
	Lindblom, Alton E.	Mankato
	Lindeland, Arthur T.	Minneapolis
	Lindell, Robert E.	St. Paul
	Lindeman, Raymond J.	Paynesville
	Lindemann, Charles E.	Minneapolis
	Linderholm, Bruce E.	Minneapolis
	Lindgren, Russell C.	Minneapolis
	Lindley, Stanley R.	Fergus Falls
	Lindquist, Dale C.	Lindstrom
	Lindquist, Janet M.	Nigera, W. Africa
	Lindquist, Max F.	South St. Paul
	Lindsay, Malcolm I., Jr.	Rochester
	Lindquist, Wesley L.	St. Cloud
£	Lindstrom, Richard L.	Minneapolis
	Linnell, L. S.	Duluth
	Linner, John H.	Minneapolis
	Linner, Paul W.	Minneapolis
#	Lippman, Harry H.	San Diego, CA
†	Lipschultz, Martin L.	Minneapolis
	Lipschultz, Oscar	Minneapolis
*†	Litkewitsch, Helene	St. Paul
†	Litman, Abraham B.	Minneapolis
†	Litman, Samuel N.	Duluth
	Litman, Thomas	Minneapolis
	Litzow, Thaddeus J.	Rochester
	Lloyd, Brian E.	Crookston
	Lo, Josephine	Minneapolis
	Lobell, Michael	St. Paul
	Lober, Paul H.	Minneapolis
	Locke, Murray S.	Minneapolis
£	Lockwood, Reed R.	Rochester
	Loeb, George L.	St. Cloud
	Loes, Louis A.	St. Cloud
§	Loes, Michael W.	Minneapolis
§	Loes, Peter L.	Minneapolis
	Lofgren, Eric P.	Rochester
	Lofgren, Karl A.	Rochester
	Lofsness, Stanley V.	Minneapolis
	Logan, George B.	Rochester
£	Logan, William S.	Rochester
	Lohmann, John G.	Pipestone
	Loken, Merle K.	Minneapolis
	Loken, Selmer M.	St. Paul
†	Loken, Theodore	Ada
	Lommen, Morris	Austin
	Lommen, Peter A., Jr.	Austin
	London, Nathaniel J.	Minneapolis
	Longfellow, Helen	Brainerd
	Lonstein, John E.	Minneapolis
	Loomis, George L.	Winona
£	Looney, Timothy	Minneapolis
	Lorentzen, Ernest S.	Detroit Lakes
	Lott, Frederick H.	Minneapolis
†	Love, J. Grafton	Rochester
	Love, Thomas A.	St. Paul
†	Lovett, Beatrice R.	Minnetonka
	Lowe, Alexander D.	South St. Paul
	Lowe, Douglass A.	Minneapolis
†	Lowe, Thomas A.	South St. Paul
	Lowry, Jeanette K.	Minneapolis
	Lowry, Paul T.	Minneapolis
	Lu, Cheng-en	Fergus Falls
	Lu, Jennie W. G.	Fergus Falls
	Luby, Thomas H.	St. Cloud
£	Lucas, Charles T.	Rochester
	Luckey, William T.	Minneapolis
	Ludes, Bernard F.	Rochester
	Lueck, Wallace W.	Minneapolis
	Lueders, James H.	Evansville
	Lufkin, Murray W.	St. Paul
*†	Lufkin, Nathaniel H.	Minneapolis
	Luh, Edwin F.	Fergus Falls
	Lukinac, Charles J.	Minneapolis
	Lukk, Olaf	Prior Lake
	Lund, George W.	Minneapolis
	Lund, J. Benjamin	Mankato
	Lund, Nancy R.	Minneapolis
	Lund, Richard R.	Minneapolis
†	Lund, Werner J.	Staples
	Lundberg, Kay R.	Duluth
	Lundberg, William I.	Duluth
	Lundblad, Rodger R.	Minneapolis
	Lundblad, Stanley W.	Minneapolis
	Lundborg, Gary T.	Bemidji
§	Lunde, Paula	Minneapolis
†	Lundeberg, Karl R.	Minneapolis
	Lundell, Carl L.	Granite Falls
†	Lundholm, Arthur M.	Princeton
	Lundquist, Charles B.	Minneapolis
	Lundquist, Curt W.	Owatonna
	Lundquist, Virgil J.	Minneapolis
	Lundsten, Leslie C.	Bemidji
	Lunseth, John B.	St. Paul
	Lunzer, Richard G.	St. Paul
§	Lupo, Virginia R.	Edina
£	Luthra, Harvinder S.	Rochester
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	Lynch, Francis W.	St. Paul
	Lynch, Michael F.	Minneapolis
	Lynch, Raymond P.	St. Paul
	Lynch, Richard P.	St. Paul
†	Lynde, Orrin G.	Los Gatos, CA
	Lynn, Hugh B.	Rochester
	Lyon, Fred A.	Minneapolis
	Lyon, John D.	Hopkins
	Lyon, Larry E.	Luverne
	Lyons, John R.	St. Cloud
	Lysyj, Anatol	Minneapolis
	Lyzenga, Anton G.	Minneapolis

M

	McAfee, David K.	Willmar
	McBean, James B.	Rochester
	McBride, Alexander M.	Mankato
	McBride, John W.	St. Paul

	McCafferty, Charles	St. Paul
	McCaffrey, F. John	Minneapolis
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	McCannel, Malcolm A.	Minneapolis
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	McCarthy, Austin M.	Willmar
	McCarthy, Charles J.	St. Paul
†	McCarthy, Donald	Minneapolis
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	McClelland, John G.	Virginia
	McCloud, C. Naumann	St. Paul
	McCollister, Robert J.	Minneapolis
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£	McConahey, William N. III	Rochester
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†	McDaniel, Samuel P.	Lakeville
	McDonald, Thomas J.	Rochester
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#	McElfresh, Edward C.	Ft. Eustis, VA
	McEllistrem, Edward J.	St. Paul
	McEllistrem, Gerald D.	St. Paul
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	McEwan, Alexander	St. Paul
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	McGill, Douglas B.	Rochester
	McGovern, Lawrence O.	Minneapolis
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	McGroarty, Brian J.	St. Paul
	McHutchison, Samuel K.	North St. Paul
	McIlrath, Donald C.	Rochester
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†	McKelvey, John L.	St. Paul
	McKelvey, John M.	Minneapolis
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	McKenna, James L.	Minneapolis
	McKenna, John J.	Virginia
†	McKenna, Jay K.	LaJolla, CA
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	McKenzie, Eva E.	St. Paul
	McKhann, Charles F.	Minneapolis
	McKinlay, Gordon L.	Minneapolis
	McKinley, C. Richard	Minneapolis
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	McLaughlin, Byron H.	Minneapolis
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	McMahon, John E.	Minneapolis
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	NcNeill, John A.	Minneapolis
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	McNeil, John A.	St. Paul
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	McParland, Felix A., Jr.	Minneapolis
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¶	McShane, Sister M. Quentin	Rochester
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†	MacDonald, Daniel A.	Minneapolis
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	MacKinnon, Donald C.	Minneapolis
†	MacLean, Alexander R.	Rochester
	MacMillan, David G.	St. Paul
†	MacRae, Gordon C.	Duluth
†	Mach, Frank B.	Minneapolis
	Mach, John R.	Minneapolis
	Mach, Ralph R.	Pine City
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	Mackoff, Samuel	Phoenix, AZ
	Madireddi, Sivarama K.	Osseo
	Madland, Robert S.	St. Paul
	Madsen, Donald O.	Minneapolis..
	Madsen, Eugene F.	Rochester
	Maeder, Edward C.	Minneapolis
	Maeder, Edward C., Jr.	Minneapolis
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	Magee, Timothy M.	Minneapolis
	Magid, Gail A.	Santa Cruz, CA
	Magnuson, Michael C.	Rochester
	Magnuson, Raymond C.	Combridge
	Magtibay, Meynardo B.	Tyler
	Maher, Frank T.	Rochester
	Maher, Thomas D.	St. Paul
	Mahle, Donald G.	Wabasha
	Mahmud, Cholid	Minneapolis
	Maitland, Edwin T.	Willmar
	Malek, Reza S.	Rochester
	Malerich, J. Anthony	Cottage Grove
	Malkasian, George D.	Rochester
	Malmquist, Carl P.	Minneapolis
	Malone, Patrick M.	Willmar
	Mandel, Sheldon L.	Minneapolis
	Manick, Kenneth P.	Minneapolis
	Mankey, James C.	Minneapolis
	Mankin, Harold T.	Rochester
	Manlove, Charles H., Jr.	St. Paul
	Mann, George A.	Minneapolis
	Manoles, Elias N.	Minneapolis
	Manolis, Deane C.	Minneapolis
	March, Barrie L.	Detroit Lakes
	Marciniak, Thomas A.	Rochester
	Marcoux, J. Paul	Rochester
	Marcus, Walter M.	Rochester
£	Marik, Francis	Rochester
	Mark, Aaron L.	Minneapolis
	Mark, Merle S.	Minneapolis
	Mark, Peter M.	Minneapolis
	Marking, George H.	Minneapolis
	Markland, Colin	Minneapolis
	Markovitz, Jack M.	Minneapolis
£	Marmer, Robert H.	Rochester
	Marshall, Clark M.	Crosby
	Marso, John L.	Mankato
	Marta, John B.	St. Paul
	Marte, Egon	Minneapolis
	Martens, Theodore G.	Rochester
£	Martimbeau, Pierre	Rochester
	Martin, Doreen A.	Pepin, WI
	Martin, Dwight L.	St. Paul
	Martin, Frank E.	Minneapolis
	Martin, Frederick F.	Bagley
	Martin, George B.	Thief River Falls
	Martin, George R.	Minneapolis

	Martin, Gordon M.	Rochester
	Martin, Harold R.	Rochester
¶	Martin, James E.	Rochester
	Martin, Maurice J.	Rochester
†	Martin, Webster C.	Duluth
	Martinson, Elmer J.	Wayzata
	Martinson, Raymond M.	Virginia
£	Maruta, Tashihiko	Rochester
	Marvin, Joseph E.	Brainerd
	Maryland, Daniel L.	Duluth
§	Masem, Mathias A.	New Brighton
	Maslansky, Robert A.	Minneapolis
£	Mason, Bruce D.	Rochester
	Massee, Joseph S.	Minneapolis
†	Masson, James C.	Rochester
	Masson, James K.	Rochester
	Mast, Frederic L.	Chisholm
	Mastbaum, Leonard T.	Minneapolis
	Mateo, Guillermo	St. Paul
	Mathers, John E.	Duluth
	Mathews, Wallace E.	Mankato
†	Mathieson, Don R.	Rochester
	Mathison, Larry A.	Fergus Falls
	Mathog, Robert H.	Minneapolis
£	Matlak, Michael E.	Rochester
	Matson, Roland W.	Spring Valley
	Matthews, John A. G.	Minneapolis
	Matthews, Marilyn	St. Paul
	Mattson, Donald S.	Willmar
	Mattson, Larry D.	Detroit Lakes
	Mattson, Roger A.	Minneapolis
	Matus, Richard N.	St. Paul
	Maunder, John B.	Minneapolis
	Maus, Donald J.	Monticello
	Maus, Philip W.	Dawson
†	Maxeiner, Stanley R.	Minneapolis
	Maxeiner, S. R., Jr.	Minneapolis
	Maxwell, Robert E.	Minneapolis
	May, Horst G.	Duluth
	May, Robert B.	St. Cloud
	Mayberg, Donald M.	Minneapolis
	Mayberry, William E.	Rochester
	Mayne, John G.	Rochester
	Mazzitello, William F.	St. Paul
	Meany, Thomas J.	Minneapolis
	Mears, Burtis J.	St. Paul
	Mears, Thomas V.	Minneapolis
	Mecklenburg, Fred E.	Minneapolis
	Medelman, John P.	St. Paul
	Medina, Ambrosio M., Jr.	Wayzata
	Meeker, Henry C.	Minneapolis
	Meekin, Patrick C.	Minneapolis
†	Meinert, Albert E.	Winona
	Meinert, John K.	Willmar
	Melancon, Joseph F.	St. Paul
	Meland, Mary H.	Minneapolis
	Melichar, Paul J.	Minneapolis
	Meller, Maurice	Brainerd
	Meller, Robert L.	Minneapolis
	Mendesh, Anthony N.	Duluth
	Mendiola, Ramon P., Jr.	Waconia
	Menefee, Edward C.	Albert Lea
	Mennis, William I.	Staples
	Mensheha, Nicholas M.	Minneapolis
	Mercil, C. B.	Mahnomen
†	Mercil, William F.	Crookston
	Merickel, Joseph	Fergus Falls
	Merner, Thomas B.	Faribault
†	Merrick, Charlotte T.	St. Paul
	Merrick, Robert L.	St. Paul
	Merrill, Robert	Des Moines, IA
	Merritt, Wallace A.	Rochester
	Mersy, David J.	Red Lake Falls
	Messenger, Michael A.	St. Paul
	Messick, Joseph M. Jr.	St. Paul
	Metcalf, Norman	Princeton
	Metz, Donald D.	Minneapolis
	Meyer, Alvin J.	Minneapolis
†	Meyer, Frederick C.	Kenyon
	Meyer, Howard J.	Duluth
	Meyer, Richard H.	Faribault
	Meyer, Robert P.	Faribault
	Michaelis, Dorothy L.	Duluth
†	Michel, Henry H.	Minneapolis
	Michels, Roger P.	Willmar
	Michienzi, Leonard J.	St. Paul
†	Mickelsen, Emma F. (Fronk)	Holmes Beach, FL
	Midboe, Gilbert T.	Forest Lake
	Middlebrook, John E.	Minneapolis
	Midthune, Andreen S.	Lake Park
	Miettunen, John B.	Hibbing
	Mijares, Wilfredo S.	Fairmont
	Miks, George M.	Aurora
£	Miles, Wayne B.	Rochester
†	Milhaupt, Emmett N.	Dunedin, FL
	Miller, Albert G.	St. Paul
	Miller, Fletcher A.	St. Paul
	Miller, H. Dawes	Minneapolis
	Miller, Harry G.	Virginia
	Miller, Harold E.	Minneapolis
	Miller, Herman	Austin
*†	Miller, Hugo E.	Minneapolis
	Miller, J. Carleton	Minneapolis
	Miller, John H.	Rochester
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	Miller, Linda K.	Winona
	Miller, James D.	Owatonna
	Miller, Roland D.	Rochester
	Miller, Ross H.	Rochester
	Miller, W. Eugene	Rochester
	Miller, William P.	Minneapolis
	Miller, Winston R.	St. Paul
	Miller, Zondal R.	Minneapolis
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	Millikan, Clark H.	Rochester
†	Mills, John L.	Winnebago
	Mills, Stephen D.	Rochester
	Milnar, Frank J.	St. Paul
	Milroy, Thomas W.	Aberdeen, SD
	Minder, John G.	Minneapolis
	Mindrum, Gerald G.	Minneapolis
	Minge, Raymond K.	Worthington
†	Minsky, Armen A.	Minneapolis
	Mintalar, Jose M.	Winsted
	Mishek, Charles J.	St. Paul
	Mitby, Irvin L.	Minneapolis
	Mitchell, Berton D.	Minneapolis
†	Mitchell, Edward C.	College Place, WA
	Mitchell, George S.	St. Paul
#	Mitchell, John C., III	Travis AFB, CA
	Mitchell, Mancel T.	Minneapolis
	Mixer, Harry W.	Minneapolis
	Mlinar, Joseph P.	Austin
	Mock, Charles J.	Virginia
	Moe, John H.	Minneapolis
	Moe, W. Wyatt	Minneapolis
	Moehn, John T.	Minneapolis

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†	Moersch, Frederick P.	Fort Lauderdale, FL
†	Moersch, Herman J.	Rochester
	Moghaddam, Alaeddin	Minneapolis
£	Mokri, Bahram	Rochester
†	Molander, Herbert A.	North St. Paul
	Molenaar, Robert E.	Cannon Falls
	Molina, J. Ernesto	St. Paul
	Moller, Julie C.	Duluth
	Moller, Jurgen	West St. Paul
	Molnar, George D.	Rochester
	Monahan, Robert H.	St. Paul
	Mongé, James J.	Duluth
	Monserud, Nels O.	Cloquet
£	Monkman, George R.	Rochester
	Monson, Einer M.	Minneapolis
	Monson, Leonard J.	Canby
	Monson, Paul S.	Mound
	Monson, Warren A.	Minneapolis
	Montaniel, Necito L.	Crookston
†	Montgomery, Hamilton	Rochester
	Moody, David L.	Minneapolis
	Mooney, Robert D.	St. Paul
	Moore, Burton A.	Rochester
	Moore, Gordon L., II	Rochester
†	Moore, Irvin H.	Eden Prairie
£	Moore, Richard H.	Bloomington
	Moorhead, Marie	Minneapolis
	Moos, Daniel J.	Minneapolis
£	Moquist, Dale C.	New Hope
	Moral, Harvey M.	Minneapolis
£	Moran, John A.	St. Paul
	Moran, Paul T.	St. Cloud
†	Morehead, Dewey E.	Bodega Bay, CA
	Moren, J. Adelaide	St. Paul
*	Morgan, Hugh O.	Amboy
	Morgan, John C.	Minneapolis
	Mori, Hideo	Grand Meadow
#	Morimoto, Allen M.	San Francisco, CA
	Mork, A. Harold	Anoka
†	Mork, Frank E.	Anoka
	Mork, Frank E., Jr.	Minneapolis
	Mork, John N.	Worthington
	Morlock, Carl G.	Rochester
£	Morrey, Bernard F.	Rochester
	Morrow, George W., Jr.	Rochester
†	Morse, Morton P.	LeRoy
	Morse, Robert M.	Rochester
	Morse, Roger D.	LeRoy
	Mortenson, Howard O.	Menahga
†	Mosby, Maurice E.	Long Prairie
	Moshfeghi, Mohammad M.	Red Wing
	Moss, Nyel H.	Minneapolis
	Mosser, Donn G.	Minneapolis
	Mossman, Philip L.	Minneapolis
	Moulton, Keith B.	St. James
	Mouritsen, Glenn J.	Fergus Falls
	Mowlem, Albert	St. Paul
	Moyer, John B.	Duluth
	Moyer, Leonard B.	Minneapolis
	Moyer, Richard R.	Hibbing
	Muchow, Gene C.	Austin
	Mueller, Donald R.	Grand Rapids
	Mueller, Henry M.	St. Paul
	Mueller, James M.	Minneapolis
	Mueller, LeRoy E.	Hendricks
	Mueller, Rudolph B.	Richmond
	Muenter, Manfred D.	Rochester
	Muesing, Mark A.	Brainerd
	Muesing, William J.	New Ulm
	Mulder, Donald W.	Rochester
	Mulder, Richard D.	Ivanhoe
	Mulford, Beatrice	St. Paul
	Mulhausen, Robert D.	St. Paul
	Mulholland, William M.	Minneapolis
	Muller, A. Eugene	North St. Paul
	Muller, John J.	Hibbing
	Muller, Sigfrid A.	Rochester
	Mullin, Gerald T., Jr.	Minneapolis
	Mulrooney, John	Winona
	Mulrooney, Thomas F.	St. Paul
	Mulvahill, John E.	Minneapolis
	Mundahl, Harold R.	St. Paul
	Munger, James E.	Duluth
	Munkittrick, Ronald C.	Minneapolis
	Munneke, Lyle	Clara City
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	Munson, Martin S.	Moose Lake
	Murdock, David K.	Minneapolis
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	Murphy, Joseph E.	Marshall
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	Murray, Robert A.	Hibbing
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	Mylrea, Murray J.	Burnsville
†	Myre, Clifford R.	Paynesville

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	Nealy, Timothy E.	Blooming Prairi
	Neault, Roger W.	Rocheste
	Neel, Harry B.	Albert Le
£	Neel, H. Bryan, III	Rocheste
	Neff, Walter S.	Virgini
	Neher, Frederick J.	St. Pau

Neils, Vernon E. ....St. Cloud
Neira, Edward H. ....St. Paul
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Nelson, David J. ....St. Paul
£ Nelson, David W. ....Minneapolis
Nelson, Delbert R. ....St. Paul
Nelson, Edward N. ....Minneapolis
Nelson, Evan L., Jr. ....Minneapolis
Nelson, Glen D. ....Minneapolis
Nelson, Glenn E. ....Redwood Falls
Nelson, Gunard A. ....Minneapolis
† Nelson, Harvey ....Deerfield Beach, FL
† Nelson, Henry E. ....Crookston
Nelson, Lloyd S. ....Mineapolis
Nelson, Loren E. ....St. Paul
Nelson, Louis A. ....St. Paul
Nelson, Luther A. ....Rush City
Nelson, Maxine O. ....Minneapolis
Nelson, Maynard C. ....Minneapolis
Nelson, O. L. Norman ....Minneapolis
Nelson, Ralph A. ....Rochester
Nelson, Robert H. ....Benson
£ Nelson, Robert P. ....St. Paul
Nelson, Ronald J. ....St. Paul
Nelson, Ronald J. ....St. Paul
Nelson, Roy A. ....Fergus Falls
Nelson, Wallace I. ....Minneapolis
Nemanich, George J. ....Minneapolis
Nerenberg, Sidney ....Minneapolis
Nerothin, Paul ....Forest Lake
Neshiem, Martin O. ....Albert Lea
Ness, Duane E. ....Wadena
Ness, Richard A. ....Fergus Falls
Nesse, Anton S. ....Minneapolis
Nesset, David G. ....Rochester
Nesset, Lawren B. ....Minneapolis
Nesset, William D. ....Minneapolis
Nesvacil, Leon ....St. Paul
Neumann, Roland F. ....Minneapolis
Neumeister, Charles A. ....Minneapolis
£ Neupert, Jerrol R. ....Rochester
Neuwirth, Gerardo D. ....Minneapolis
Newcomber, Albert D. ....Rochester
Niazi, Suad A. ....Granite Falls
Nicholas, S. Scott, Jr. ....Minneapolis
Nichols, Donald R. ....Rochester
Nichols, Thomas O. ....St. Paul
Nichols, Victoria R. ....Rochester
Nicholson, Richard W. ....Fergus Falls
Nickerson, John R. ....Faribault
Nickerson, Neil D. ....Fairmont
Nicolette, Charles C. ....Minneapolis
Nicolosi, Charles S. ....Red Wing
Nielsen, David J. ....Minneapolis
Nietfeld, Aloys B. ....Sauk Centre
£ Nijensohn, Daniel E. ....Rochester
Nilsen, John A. ....Minneapolis
Nimlos, Lenore O. ....St. Paul
Nisius, George F. ....Duluth
Nivatvongs, Santhat ....Minneapolis
£ Niven, Robert G. ....Rochester
Nisswandt, Albert L. ....Duluth
Nixon, James B. ....Crosby
Nobrega, Fred T. ....Rochester
£ Nolan, Declan R. ....Rochester
Nolan, Robert K. ....Minneapolis
Nolen, William A. ....Litchfield
Nollet, Donald J. ....Hibbing
Noran, Harold H. ....Minneapolis
† Norberg, Carl E. ....Los Altos, CA
Norberg, William J. ....Minneapolis
Nord, Robert E. ....Minneapolis
Nordman, Willard F. ....Mora
Norman, David D. ....St. Paul
Norman, Franklin C. ....Minneapolis
Norman, Mark L., Jr. ....Minneapolis
Normann, Stephen T. ....Waseca
Norquist, Joseph L. ....St. Paul
Norris, John C. ....Mankato
Norval, Mildred A. ....Minneapolis
† Nuessle, Walter G. ....Springfield
Nuessle, William F. ....Minneapolis
Nussbaum, Daniel ....Minneapolis
Nydahl, Bruce C. ....Minneapolis
† Nydahl, Malvin J. ....Sun City, AZ
† Nygren, William T. ....Braham
Nywall, Dean D. ....Slayton

O

O'Brien, Bruce J. ....Minneapolis
£ O'Brien, Daniel K. ....Minneapolis
O'Brien, Gerald R. ....Minneapolis
O'Brien, John C. ....St. Paul
O'Brien, Louis T. ....Breckenridge
O'Brien, William A. ....Minneapolis
O'Byrne, Alvaro ....Mankato
£ O'Dea, Michael J. ....Rochester
† O'Donnell, James E. ....Minneapolis
O'Hanlon, William J. ....Minneapolis
O'Kane, Thomas W. ....St. Paul
O'Keefe, James P. ....St. Cloud
O'Leary, John B. ....Minneapolis
O'Malley, Valentine ....St. Paul
O'Neil, Bernerd L. ....Minneapolis
O'Neill, John C. ....Duluth
O'Neill, Nial C. ....St. Paul
O'Phelan, E. Harvey ....Minneapolis
† O'Reilley, Bernard E. ....Sun City, AZ
O'Rourke, William J. ....Austin
Obetz, Samuel W. ....Rochester
Ockuly, Orville E. ....St. Paul
Odland, Donald M. ....Luverne
Odland, Mark E. ....Detroit Lakes
Odland, Olin M. ....Marshall
£ Odyniec, Norman A. ....Rochester
Oeljen, Siegfried C. ....Waseca
Officer, Charles D. ....Burnsville
† Ogden, Warner ....River Falls, WI
§ Ogle, Richard G. ....Lakeville
† Ohage, Justus ....St. Paul
Ohmann, Ronald J. ....Minneapolis
Ohrt, D. K. ....Mankato
Okagaki, Takashi ....Minneapolis

	Olavs, Olga	Minneapolis
	Olds, George H.	New Richland
	Olfelt, Paul C.	Minneapolis
	Olinger, John N.	St. Cloud
£	Olivet, Ronald T.	Rochester
#	Ollila, Eugene W.	Grand Forks
*†	Olmanson, Edmund G.	St. Peter
	Olmanson, M. Donald	St. Peter
	Olmanson, Vern C.	St. Peter
	Olsen, Arthur M.	Rochester
†	Olsen, E. George	Minnetonka
	Olsen, Jay R.	Minneapolis
	Olsen, Ralph L.	St. Paul
	Olson, Albert J.	Owatonna
	Olson, Alton C.	Minneapolis
	Olson, Barbara F.	Minneapolis
	Olson, C. Kent	Minneapolis
	Olson, Carl J.	Minneapolis
	Olson, Clyde R.	Duluth
£	Olson, David J.	Minneapolis
	Olson, Detlof M.	Minneapolis
	Olson, Duane C.	Minneapolis
†	Olson, Frances P.	Fergus Falls
	Olson, Grant E.	West Concord
	Olson, Gregory M.	Litchfield
	Olson, Hardin E.	Minneapolis
	Olson, John D.	Rochester
	Olson, Lillian A.	Bertha
	Olson, Neal R.	Rochester
	Olson, Philip A.	Minneapolis
	Olson, Philip K.	Minneapolis
§	Olson, Richard A.	Minneapolis
	Olson, Richard E.	Chaska
	Olson, Richard T.	Virginia
	Olson, Robert A.	Minneapolis
	Olson, Robert E.	Minneapolis
	Olson, Robert T.	Canby
	Olson, Robert W.	Minneapolis
	Olson, Rolland A.	Wayzata
	Onofrio, Burton M.	Rochester
†	Onsgard, L. Kenneth	St. Petersburg, FL
	Opheim, Richard H.	Minneapolis
	Opitz, Joachim L.	Rochester
†	Oppegaard, C. L.	Scottsdale, AZ
†	Oppen, E. Gerhard	Minneapolis
	Oppen, Melvin G.	Minnetonka
	Opsahl, Lawrence J.	Willmar
	Opstad, Earl T.	Minneapolis
	Orandi, Ahmad	Fergus Falls
	Orandi, Mehdi	Fergus Falls
	Orbuch, Martin W.	Minneapolis
	Orkin, Milton	Minneapolis
	Orn, Duane L.	Minneapolis
	Orr, Burton A.	Faribault
	Orr, Ernest W.	St. Paul
	Ortegon, Pedro R.	Crookston
	Osborn, Donald	Austin
	Osekowsky, Henry J.	St. Paul
	Osmundson, Philip J.	Rochester
	Osteraas, Grayson R.	St. Cloud
	Osterberg, Kenneth A.	Minneapolis
£	Ostergaard, Daniel J.	Duluth
†	Ostergaard, Erling	Elbow Lake
	Ostrov, Charles S.	Minneapolis
	Ott, Eugene C.	Minneapolis
	Ouellette, Alfred J.	St. Paul
	Ourada, Anthony L.	Buffalo
	Overgaard, Peter H., Jr.	Lindstrom
	Owen, Charles A., Jr.	Rochester
	Owen, Richard R.	Minneapolis
	Owens, Ben P.	Hibbing
	Owens, Frederick M.	St. Paul
	Owens, William A.	Montevideo
#	Oxman, Herbert A.	San Antonio, TX

P

	Paal, Dwain J.	Minneapolis
	Paciotti, Vincent J.	Hibbing
	Padilla, Cerferanio B. Jr.	St. Paul
†	Page, Raymond L.	St. Paul
	Paguyo, Nelson	So. St. Paul
	Paisner, Hyman M.	Minneapolis
†	Palen, Benjamin J.	Scottsdale, AZ
	Palm, Neil M.	St. Paul
†	Palmer, Clinton F.	Albert Lea
	Palmer, Harry A.	Blackduck
	Palumbo, Pasquale J.	Rochester
	Pangaloss Anastase	St. Paul
	Panning, Wayne P.	Marshall
	Paparella, Michael M.	Minneapolis
	Papermaster, Ralph	St. Louis Park
	Papermaster, Theodore C.	Minneapolis
†	Park, Wilford E.	Minneapolis
	Parker, Robert L.	Rochester
	Parker, Warren E.	Sebeka
	Parker, Wilbert H.	Chisholm
†	Parkhill, Edith M.	Rochester
	Parod, John D.	Minneapolis
	Parra, Samuel	Crookston
	Parrott, John C.	Minneapolis
#	Parry, Rodney R.	Rochester
	Parson, E. Irvine	Duluth
†	Parson, E. Lillian	Elbow Lake
	Parsons, R. A.	St. James
	Parsons, Ralph L.	Trimont
	Pasek, Antone W.	Cloquet
	Pass, Franklin	Minneapolis
	Patch, Orien B.	Duluth
	Pattee, James J.	Minneapolis
	Patten, John C.	Austin
	Patterson, Hugh D.	Slayton
¶	Patterson, Linda G.	Fargo, ND
	Patterson, Paul G.	Minneapolis
	Paule, William J.	Minneapolis
	Paulson, Elmer C.	St. Paul
£	Paulson, Olaf B.	Rochester
	Paulson, Wallace J.	St. Paul
£	Payne, Eliz E.	Minnetonka
	Payne, Richard E.	Virginia
	Payne, W. Spencer	Rochester
	Peake, Janna Z.	St. Paul
	Pearson, Bror F.	Shakopee
†	Pearson, Fritz R.	St. Paul
	Pearson, Harris L.	Bagley
	Pearson, Jack W.	Fergus Falls
	Pearson, Malcolm M.	St. Paul

† Pease, Gertrude L. ....Rochester
† Pedersen, Arthur H. ....St. Paul
Pedersen, Robert L. ....Brainerd
Peikert, Carl F. ....Forest Lake
Pelletier, Rene W. ....St. Paul
Peluso, Charles R. ....Minneapolis
Pelzl, Charles R. ....Pine River
Penk, Engward L. ....Springfield
Pennington, Mary ....Minneapolis
Peper, Martin C. ....Minneapolis
Perkins, Douglass E. ....Alexandria
Perlman, Everett C. ....Minneapolis
Perlman, Herschel L. ....St. Louis Park
Perry, Harold O. ....Rochester
£ Perry, Michael C. ....Rochester
Perry, John F., Jr. ....St. Paul
Perry, Lawrence B. ....Rochester
Person, Duane F. ....Virginia
Pesonen, Clifford ....Austin
Peteler, Jennings, C. L. ....Minneapolis
Peters, Gustavus A. ....Rochester
£ Peters, John R. ....Minneapolis
Petersen, Byron D. ....Minneapolis
Petersen, Deane A. ....Wayzata
Petersen, Donald H. ....Willmar
£ Petersen, Eugene G. ....Rochester
Petersen, Glenn L. ....Minneapolis
£ Petersen, Kenneth ....Portland, OR
† Petersen, Magnus C. ....Rochester
Petersen, Robert T. ....St. Cloud
Petersen, William E. ....Minneapolis
Peterson, Alvin C. ....Mora
Peterson, Charles A. ....Minneapolis
Peterson, Charles R. ....Minneapolis
Peterson, Donald H. ....St. Paul
Peterson, Edward A. ....St. Paul
† Peterson, Edward N. ....Virginia
£ Peterson, Garry ....St. Paul
Peterson, Hamlet A. ....Rochester
Peterson, Harold O. ....Minneapolis
Peterson, John A. ....Minneapolis
Peterson, John H. ....Duluth
Peterson, John R. ....Rushford
Peterson, Kenneth A. ....Marshall
Peterson, Kenneth H. ....Hutchinson
Peterson, Lowell F. A. ....Rochester
Peterson, Norman P. ....Duluth
Peterson, Oliver H., Jr. ....Minneapolis
Peterson, Palmer A. ....Minneapolis
Peterson, Rodney H. ....Minneapolis
† Peterson, Roy A. ....Vesta
Peterson, Roy L. ....White Bear Lake
£ Peterson, Stanley C. ....Sun City, AZ
Peterson, Theodore A. ....Minneapolis
Peterson, Willard C., Jr. ....Minneapolis
Peterson, Willard E. ....Willmar
Petit, Julien V. ....Minneapolis
*† Petit, Leon J. ....Minneapolis
Petitt, Robert M. ....Rochester
Pettersen, George R. ....Rochester
† Petraborg, Harvey T. ....Aitkin
Pettko, Joseph ....Wheaton
Pewters, John T. ....Minneapolis
Peyla, Thomas L. ....Rochester
Pafaffenbach, David D. ....Ft. Sam, TX
Pfeffer, David W. ....Duluth
Pfeiffer, Craig N. ....Rochester
Pfohl, Richard A. ....Minneapolis
Phares, Otto C. ....St. Cloud
† Phelps, Kenneth A. ....Palo Alto, CA
Phelps, Robert D. ....Minneapolis
Phibbs, Clifford M., Jr. ....Minneapolis
Phillips, Leonard ....St. Paul
Philp, David R. ....Watertown
Pierre, Robert V. ....Rochester
Pierson, Roy F. ....Slayton
£ Pietan, Jerold H. ....Rochester
Pikler, George M. ....DeRidder, LA
Pilling, Loran F. ....Minneapolis
Pilney, Frank T. ....St. Paul
Pincus, Mitchell ....Minneapolis
Pinsonneault, W. A. ....Warren
Pistulka, Rolland D ....Chaska
Pitcher, Arlo L. ....St. James
Pitzele, Charles E. ....St. Paul
Pivac, Dragojla (Popovich) ....Milwaukee, WI
Pizarro, Remi L. ....Minneapolis
Plasha, Matt K. ....Coon Rapids
Plass, Herbert F. R. ....Minneapolis
Pleissner, Karl W. ....Minneapolis
Plimpton, Nathan C. ....Minneapolis
Plotke, Harry L. ....St. Paul
Plucker, Milton W. ....Worthington
Pluth, James R. ....Rochester
£ Plutnicki, Ronald S. ....Rochester
Pogue, Charles G. ....Albert Lea
Pohl, John F. ....Minneapolis
£ Poland, Jerome D. ....Minneapolis
Polesky, Herbert F. ....Minneapolis
Poljack, Stuart James ....Minneapolis
Poley, Brooks J. ....Minneapolis
Pollak, Kurt ....Minneapolis
Pollard, William S. ....Duluth
Polley, Howard F. ....Rochester
Pollock, Anthony J. ....Minneapolis
Polski, Paul G. ....South St. Paul
*† Polzak, James A. ....Roseville
† Pone, John J. ....Shakopee
Ponterio, James E. ....Shakopee
† Pool, T. Lloyd ....Rochester
Poole, James R. ....Wheaton
Popadiuk, Peter ....Minneapolis
Popoff, Russel G. ....Graceville
Popowich, John G. ....Minneapolis
Poppie, Robert W. ....Brainerd
£ Port, Friedrich K. ....Rochester
Post, Edmund A. ....St. Paul
Poston, Lawrence M. ....Caledonia
Potter, Robert B. ....Minneapolis
Pougiales, Mary L. ....Rochester
Power, John E. ....Duluth
Powers, Robert L. ....St. Paul
£ Prakash, Udaya B. S. ....Rochester
† Pratt, Fred J. ....Minneapolis
Pratt, Joseph H., Jr. ....Rochester
Prawer, Steven E. ....Minneapolis
Prem, Konald A. ....Minneapolis
Prentice, James A. ....Rochester
Preston, Frank S., Jr. ....Minneapolis
Price, William E. ....Minneapolis
† Prickman, Louis E. ....Rochester
Prickman, William E. ....Minneapolis
Priest, Robert E. ....Minneapolis
† Priestley, James T. ....Rochester
Prlina, Issac M. ....Virginia
Prokstfield, Jeffrey L. ....Minneapolis
Proeschel, Ray K. ....Willmar
Proshek, Lumir C. ....Minneapolis

	Provence, Cecil L.	Norwood
	Proud, Harry S.	St. Paul
	Pruitt, Raymond D.	Rochester
†	Pugh, David G.	Sun City, AZ
	Pulido, Ernesto D.	Fergus Falls
	Purdie, James L.	Forest Lake
	Purnell, Don C.	Rochester
	Purves, G. Harland	Buffalo
	Puumala, Barbara M.	Cloquet
	Puumala, Reino H.	Cloquet
	Puumala, Ricard R.	Cloquet
£	Pyle, Robert B.	Minneapolis

Q

	Quast, John E.	St. Paul
	Quattlebaum, Frank W.	St. Paul
	Quello, Robert O. B.	Minneapolis
	Quick, Cedric A.	Minneapolis
	Quiggle, Arthur B.	Minneapolis
	Quinn, Paul V.	Stillwater
£	Quiroz, Salvador E.	Rochester
	Quist, Henry W., Jr.	Minneapolis

R

	Raab, David E.	Minneapolis
	Raaen, Olaf J.	St. Paul
	Rabcevich, Anatole	St. Paul
	Racer, Harley J.	Minneapolis
	Radke, Robert L.	Milan
	Raetz, Sylvester J.	Maple Lake
	Rafferty, Dwight K.	St. Paul
	Rafferty, Robert F.	St. Cloud
	Ragan, John R.	Minneapolis
£	Rahimi, Abbas	Rochester
	Raich, John J.	Minneapolis
	Raile, Richard B.	Minneapolis
	Raimundo, Hugo S.	Rochester
	Ralph, James R.	St. Paul
	Ralston, Donald E.	Rochester
	Ramirez-Lassepas, Manuel	St. Paul
	Ramlow, Ralph M.	West St. Paul
£	Ramos, Marcos	Minneapolis
	Randall, David A.	Minneapolis
	Randall, Philip S.	Minneapolis
	Randall, Raymond V.	Rochester
	Ranheim, Phillip J.	Minneapolis
	Ransom, H. Robert	St. Cloud
£	Rasmussen, Richard W.	Rochester
	Ratelle, Alexander E.	Minneapolis
	Raths, Otto N., Jr.	St. Paul
	Rauenhorst, John M.	St. Paul
	Ravits, Harold G.	St. Paul
	Ray, Charles D.	Minneapolis
	Rayer, Anthony L.	Babbitt
	Rayner, Ralph R.	Red Wing
	Rea, Charles E.	St. Paul
	Reardon, Andrew E.	Duluth
	Recht, Thomas M.	Minneapolis
	Redleaf, Paul D.	St. Paul
	Reeber, Erick	Bagley
	Reece, Richard L.	Minneapolis
	Reed, Henry H.	Duluth
	Reed, John H., Jr.	Minneapolis
	Reed, Paul	Virginia
	Reed, Sheldon C.	Minneapolis
	Reff, Alan R.	Crookston
	Regan, John J.	Minneapolis
£	Regan, John J. Jr.	Minneapolis
	Rehmann, Ronald E.	Coon Rapids
	Reichel, Samuel M.	Minneapolis
	Reichelt, Leland G.	Wadena
	Reichert, John A.	Minneapolis
	Reick, Robert R.	Rochester
	Reid, Howard C.	Bemidji
*	Reid, James W.	South St. Paul
	Reif, Harold A.	Minneapolis
	Reif, Robert W.	White Bear Lake
	Reiley, Richard E.	Minneapolis
	Reiners, Gary L.	Cambridge
	Reinhardt, James H.	Alexandria
	Reinhart, Richard O.	Minneapolis
	Reisdorf, George E.	Minneapolis
	Reiser, Milton P.	Minneapolis
	Reitemeier, Richard J.	Rochester
	ReMine, William H., Jr.	Rochester
	Remole, William D.	Minneapolis
	Remucal, H. C.	Hutchinson
	Resch, Joseph A.	Minneapolis
	Restall, Charles J.	Rochester
	Reul, Thomas W.	Robbinsdale
	Reynolds, Dermot F.	Hibbing
	Reynolds, James F.	Minneapolis
	Rholl, Arnold O.	Minneapolis
†	Rice, Carl O.	Minneapolis
	Rice, Edwin G.	Minneapolis
	Rice, Fred A.	Minneapolis
†	Rice, Hagbart G.	Park Rapids
	Rice, William H.	St. Cloud
†	Richards, William B.	St. Cloud
	Richardson, Edward J.	St. Paul
	Richardson, Robert J.	Minneapolis
†	Richdorf, Lawrence F.	Minneapolis
	Richmond, Harvey S.	Minneapolis
	Richter, David J.	Virginia
	Richter, Paul H.	Fergus Falls
	Rick, Paul F. W.	St. Paul
	Rierson, Phillip A.	Minneapolis
	Rieschl, Elizabeth K.	Jordan
	Rifat, Baseem M.	Clarkfield
	Rife, Charles C.	Rochester
£	Rigatuso, Joseph L.	St. Paul
	Riley, Fenwick C., Jr.	Rochester
	Riley, John D.	Minneapolis
	Rimas, Matthew J.	Comfrey
	Ringhofer, Lawrence	New Ulm
†	Ringle, Otto F.	Walker
	Rinkey, Eugene	St. Paul
	Riordan, Elsie M.	Minneapolis
†	Ripple, Rudolph J.	St. Paul
	Ripple, Rudolph J., Jr.	Minneapolis
	Risch, Ronald E.	Minneapolis
	Risser, Alden F.	Stewartville
	Ritchie, Donald A.	St. Cloud

†	Ritt, Albert E.	St. Paul
	Ritter, Donald G.	Rochester
	Rivan, Robert J.	Rochester
£	Rivers, Thomas A.	Rochester
	Rizer, Dean K.	Minneapolis
	Roach, Charles A.	St. Paul
	Roach, Donald E.	St. Paul
†	Robb, Edwin F.	Minneapolis
	Roberts, Byron H.	Minneapolis
	Roberts, George A.	Austin
	Roberts, Lewis J.	Minneapolis
†	Roberts, Oliver W.	Owatonna
	Robertson, Dennis M.	Rochester
†	Robertson, Paul A.	Austin
£	Robertson, Robert C.	Rochester
	Robinson, Cortland O.	Minneapolis
£	Robinson, Gerald N.	Rochester
	Robnik, Spencer L.	Willmar
	Rock, William H.	Anoka
	Rocknem, Robert E.	Minneapolis
	Rockwell, Curtiss V.	Minneapolis
	Rockwood, Philo H.	Fergus Falls
	Rodarte, Joe R.	Rochester
	Rodgers, Richard S.	Minneapolis
	Rodman, William W.	Coon Rapids
£	Rodning, Charles B.	St. Paul
†	Roehlke, Arthur B.	Elk River
	Roemer, Henry J.	Winona
	Rogers, Charles W.	Winona
	Rogers, John R.	Rochester
£	Rogers, Roy S., III	Rochester
	Rogin, Norton	Minneapolis
†	Rogne, W. G.	Spring Grove
†	Roholt, Christian	McIntosh
	Roholt, Hartvig B.	Bemidji
†	Rohrer, Christian A.	Madison Lake
	Rohrmann, Charles A. Jr.	Minneapolis
*	Rolig, David H.	West St. Paul
	Rollins, Pat	Minnetonka
	Rome, Howard P.	Rochester
£	Rome, Jeffrey	Rochester
	Romero, Jose B.	St. Paul
	Romness, Kenneth B.	Mound
	Rooke, E. Douglas	Rochester
	Rorem, Joseph A.	Appleton
	Rose, Cordt	Albert Lea
	Rose, Robert J.	Park Rapids
	Rosenbaum, Alan H.	Rochester
	Rosenbaum, David L.	Minneapolis
	Rosenberg, Laurence J.	Wayzata
	Rosenberg, Robert H.	Minneapolis
	Rosendahl, Frederick G.	Minneapolis
†	Rosenfield, Abraham B.	Minneapolis
	Rosenow, Edward C., III	Rochester
	Rosenow, John H.	Minneapolis
	Rosenquist, Rudolph J.	Minneapolis
	Rosenstein, Hanan J.	Minneapolis
†	Rosenthal, F. Harold	Austin
†	Rosenthal, Robert	St. Paul
*†	Rosenwald, Reuben M.	Anoka
	Rosevear, John W.	Minneapolis
	Ross, James V., Jr.	Rochester
	Rossberg, Raymond A.	Morris
	Rossen, Ralph X.	Minneapolis
	Rotenberg, Robert J.	Minneapolis
	Rotenberg, Samuel	Beverly Hills, CA
	Roth, Albert H.	Deer River
	Roth, Charles W.	Red Wing
	Roth, Frederick D.	Mankato
	Rothnem, Morris S.	Minneapolis
	Rotta, James R.	Minneapolis
	Roust, Henry A.	Montevideo
	Rovelstad, Randolph A.	Rochester
	Rovelstad, Roger A.	St. Cloud
	Rowe, Clarence J., Jr.	St. Paul
	Rowe, Richard G.	Duluth
†	Rowles, Everett C.	Laguna Hills, CA
	Roy, Paul H. J.	Quebec, Canada
	Roy, Philemon C.	St. Paul
	Roy, Philemon C. Jr.	St. Paul
	Rozeboom, Paul E.	Mankato
	Rozycki, Anthony T.	St. Cloud
	Rubin, Manly	Minneapolis
	Ruchie, Warren H.	Willmar
†	Rucker, Charles W.	Rochester
	Rucker, Thomas K.	Minneapolis
†	Rucker, William H.	Minneapolis
†	Rud, Norman E.	Edina
	Rud, Paul D.	Luverne
	Rudie, Peter S.	Duluth
	Rudie, William D.	Duluth
†	Ruggles, George M.	Forest Lake
	Ruhe, Albert H.	Willmar
	Ruiz, Ernest	Minneapolis
*	Rukavina, John G.	St. Paul
*†	Rumpf, Carl W.	Faribault
	Runquist, John M.	Duluth
	Runquist, Richard K.	Cambridge
	Rushay, Arthur J.	White Bear Lake
	Rushton, Joseph G.	Rochester
†	Russ, Homer H.	Blue Earth
	Russeth, Arthur N.	Wayzata
†	Rusten, Elmer M.	Minneapolis
	Rusterholz, Alan P.	St. Paul
	Ruth, Bradley R.	Duluth
	Rutledge, John B.	Detroit Lakes
*†	Rutledge, Lloyd H.	Detroit Lakes
£	Ryan, Dennis K.	Rochester
	Ryan, Edward A.	Duluth
†	Ryan, John J.	St. Paul
	Ryan, Joseph M.	St. Paul
	Rydberg, John S.	Coon Rapids
	Ryding, Vincent	Ames, IA
	Rydland, Arne D.	Minneapolis
	Rygh, Harold N.	Atwater
†	Rynearson, Edward H.	Rochester
	Rysgaard, George N.	Northfield

S

	Sadd, Milton	Willmar
†	Saffert, Cornelius A.	New Ulm
	St. Cyr, Harry M.	Minneapolis
§	St. Cyr, John A.	Minneapolis
†	St. Cyr, Kenneth J.	Robbinsdale
	Salassa, Robert M.	Rochester
	Salchert, John J.	Minneapolis
	Salk, Richard J.	Albany
†	Saliterman, Bernard I.	Minneapolis
	Saloum, Lucille M.	Duluth
	Salovich, Edward L.	Minneapolis
	Salovich, Elmer R.	Minneapolis
†	Salter, Reginald A.	Virginia

	Salter, Wilson M.	Willmar
	Sanchez, Jose S.	West St. Paul
	Sand, Richard E.	St. Paul
	Sandeen, Robert M.	Buffalo
	Sander, Frank V., Jr.	Rochester
	Sander, John L.	Red Wing
	Sanders, Paul S.	Babbitt
	Sanderson, David J.	Fergus Falls
	Sanderson, David R.	Rochester
	Sandkamp, Virgil A.	South St. Paul
	Sandok, Burton A.	Rochester
	Sandt, Karl E.	Minneapolis
	Sane, Kumud S.	Minneapolis
	Sane, Shashikant M.	Minneapolis
†	Sanfelippo, Peter M.	Rochester
	Sanfilippo, Sylvester J.	Minneapolis
	Sanford, John B.	Duluth
	Sanford, Raymond A.	Mankato
	Sartor, Richard	Minneapolis
£	Satava, Richard M.	Rochester
	Sather, Edgar L.	Fosston
	Sather, George A.	Fosston
	Sather, Richard N.	Fosston
	Sather, Russell O.	Crookston
	Sauer, Jean C.	Fort Snelling
	Sauer, Robert L.	Preston
	Sauer, William G.	Rochester
	Savett, Laurence A.	St. Paul
	Sawtell, Robert R.	Rochester
	Sawyer, Glen T.	Minneapolis
	Sax, Milton H.	Duluth
	Saxena, Krishna M.	St. Paul
	Saxena, Kusum	St. Paul
	Saxman, Gertrude E. O.	Ulen
	Sayther, Keith D.	Minneapolis
	Sborov, Abe M.	Minneapolis
	Scallen, Raymond W.	Minneapolis
	Scanlan, John M.	St. Paul
	Scanlan, Patrick J.	Minneapolis
	Scanlan, Timothy M.	Melrose
	Scanlon, Hugh A.	Little Falls
	Scanlon, Paul W.	Rochester
	Schaar, Frances E.	Minneapolis
†	Schade, Frederick L.	Santa Cruz, CA
†	Schaefer, Joseph F.	Sun City, AZ
†	Schaefer, Wesley G.	Minneapolis
	Schafer, Charles F.	Winona
£	Schafermeyer, Robert W.	Rochester
	Schaffhausen, George E.	St. Paul
	Schaffhausen, Irwin F.	Minneapolis
	Schaffhausen, Mildred	Minneapolis
	Schamber, Walter F.	St. Cloud
£	Scheidt, William E.	Minneapolis
	Scherek, Jerome J.	St. Paul
	Scherer, L. Raymond	Minneapolis
	Scherling, Sidney S.	Minneapolis
	Scheuneman, Allen F.	Thief River Falls
	Schiele, Burtrum C.	Minneapolis
£	Schiller, Philip J.	Minneapolis
†	Schimelpfenig, George T.	Chaska
	Schindler, Richard J.	Austin
	Schirber, Martin J.	Grand Rapids
	Schirger, Alexander	Rochester
#	Schissel, Gregory A.	Washington, D.C.
	Schissel, Richard C.	Minneapolis
	Schloff, Ivan	St. Paul
	Schloff, Leonard D.	St. Paul
	Schlorf, Richard A.	St. Cloud

	Schmerler, Michael	Rochester
	Schmid, John F.	Duluth
†	Schmidt, Hilmar R.	Winona
	Schmidt, Paul G.	Granite Falls
	Schmidt, Ruben F.	Alden
	Schmidt, W. Robert	Minneapolis
	Schmidtke, Reinhardt L.	St. Paul
†	Schmitt, S. C.	Fallbrook, CA
	Schmitt, Tim B.	Browerville
	Schmitz, Anthony A.	Mankato
	Schmitz, Everett J.	St. Cloud
	Schnabel, Norma B.	Crookston
	Schnabel, Robert F.	Crookston
	Schneck, Jack I.	Minneapolis
†	Schneider, Laurence E.	Duluth
	Schneider, Sally L.	Rochester
	Schnell, Frederick S.	Litchfield
	Schochet, H. Laurence	St. Paul
£	Schoenberg, Bruce S.	Baltimore, MD
	Schoenberger, P. B.	Perham
	Schoening, Herbert A.	Minneapolis
	Schoenwetter, William F.	Minneapolis
	Schoewe, Richard W.	St. Paul
	Scholz, Donald A.	Rochester
†	Schons, Edward	Minnetonka Beach
	Schossow, George W.	White Bear Lake
	Schottler, Jerry L.	Minneapolis
*†	Schottler, Max E.	Minneapolis
	Schotzko, John R.	Blue Earth
	Schroeckenstein, Hugo F.	St. Paul
	Schroeder, Albert J.	Minneapolis
	Schroeder, Glenn E.	Red Wing
	Schroeder, William R.	No. St. Paul
	Schroeppel, Roger O.	Redwood Falls
£	Schroeter, Arnold L.	Rochester
	Schulberg, Verne A.	Minneapolis
	Schulenberg, Robert N.	Red Wing
	Schultz, Alan K.	Minneapolis
	Schultz, Alvin L.	Minneapolis
	Schultz, J. Harold	Minneapolis
	Schultz, Paul E.	St. Paul
†	Schultz, Peter J.	Minneapolis
	Schultz, Robert J.	Minneapolis
	Schulz, Jerome E.	Stillwater
	Schulze, William M.	Minneapolis
	Schumacher, John W.	Minneapolis
£	Schumacher, Robert V.	Minneapolis
	Schut, Lawrence J.	Minneapolis
	Schutt, Allan J.	Rochester
	Schutt, Ann H.	Rochester
¶	Schwartau, Neal W.	Rochester
	Schwartz, Carl A.	Hastings
	Schwartz, E. Robert	Minneapolis
	Schwartzkopff, Othild	St. Paul
	Schweiger, Theodore R.	Hibbing
	Schwinghamer, Thomas G.	Ely
¶	Schwerman, Earl A., Jr.	Rochester
£	Sciallis, Gabriel F.	Rochester
	Sciarra, John J.	Minneapolis
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	Scott, Eugene E.	St. Paul
	Scott, Horace G.	Minneapolis
¶	Scott, James J.	Rochester
£	Scott, John C.	Minneapolis
	Scott, Robert H.	Minneapolis
	Scott, William R.	Minneapolis
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	Sears, Martin E.	Fairmont

	Seay, James E., III	Minneapolis
#	Sebrechts, Paul	San Diego, CA
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	Seery, Thomas	Rochester
	Segal, Edward L.	Minneapolis
	Segal, Martin A.	Minneapolis
	Segal, Marvin S.	Minneapolis
	Segal, Sheldon J.	Minneapolis
	Segura, Joseph W.	Rochester
†	Seham, Max	St. Paul
	Seifert, Donald R.	Little Falls
	Seifert, Gregory L.	Excelsior
	Seifert, Milton H., Jr.	Excelsior
	Seisler, Edward P.	Worthington
	Sekhon, Mohan S.	St. Paul
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	Seljeskog, Edward L.	Minneapolis
	Sells, Richard J.	St. Paul
	Semba, Thomas	Minneapolis
	Semsch, Robert D.	Wayzata
#	Serafano, Donald N.	Davis-Monthan AFB, AZ
	Sessler, Alan D.	Rochester
	Sethre, Arthur E.	Fergus Falls
	Setness, Peter	Forest Lake
†	Setzer, Hobert J.	St. Paul
	Severseike, Odean M.	Minneapolis
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	Seymour, John L.	Minneapolis
	Shackelford, Terry C.	Minneapolis
	Shah, Popattal S.	Osseo
	Shah, Rangana N.	Minneapolis
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	Shandorf, James F.	Minneapolis
	Shanks, James R.	Minneapolis
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	Shapiro, Sidney K.	Minneapolis
	Shapiro, Stanley W.	Minneapolis
	Shattuck, Clark A.	Minneapolis
	Shaver, Ward	Fergus Falls
	Shaw, Howard A.	Minneapolis
	Shea, Andrew W.	Minneapolis
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	Shear, Howard H.	St. Paul
£	Sheehan, Joseph C. M.	Rochester
	Shelander, Marcus I.	St. Paul
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	Shepard, Richard	Albert Lea
	Sheppard, Charles G.	St. Peter
	Sheps, Sheldon G.	Rochester
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	Sherman, Alfred G.	Albert Lea
†	Sherman, Carnot H.	Bayport
	Sherman, Lloyd F.	Minneapolis
	Sherman, Royal V.	Red Wing
	Shick, Richard M.	Rochester
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	Shin, Rok	Howard Lake
	Shirley, Raymond M.	Duluth
	Sholler, Lawrence J.	Minneapolis
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	Shragg, Robert I.	Minneapolis
	Shronts, John F.	Minneapolis
	Shronts, John S.	Minneapolis
	Sidell, Franklin D.	Minneapolis
£	Sidell, Peter M.	Rochester
	Siebert, Darrell W.	Luverne
	Siebert, Richard C.	Minneapolis
	Siegel, Clarence	West Palm Beach, Fl.
	Siegel, John S.	Virginia
	Siegel, Leighton G.	St. Paul
	Siegmann, William C.	Minneapolis
	Siekert, Robert G.	Rochester
	Sigelman, Robert J.	Minneapolis
	Sigel, Melvin E.	Minneapolis
	Silas, Ralph M.	Minneapolis
	Silver, John D.	Minneapolis
	Silverstein, Murray N.	Rochester
	Silverstein, Paul M.	Minneapolis
	Simison, Carl	Barnesville
	Simmonds, Harry N. L.	St. Paul
	Simmons, Richard K.	Minneapolis
	Simmons, Richard L.	Minneapolis
	Simo, Kathleen Kay	Minneapolis
	Simons, Leander T.	St. Paul
	Simonson, Donald B.	Minneapolis
§	Simonson, Richard G.	Minneapolis
	Simso, Lee A.	Minneapolis
	Singer, Benjamin J.	St. Paul
	Singher, Lawrence J.	Minneapolis
	Sinykin, Melvin B.	Minneapolis
	Sipe, James W.	Minneapolis
	Siruno, Eugenio S.	Minneapolis
	Sisk, Harvey E.	St. Cloud
†	Sisler, Clifford E.	Grand Rapids
	Sjoding, J. Donald	Mankato
†	Sjostrom, Lawrence E.	St. Peter
	Skaife, W. F.	Benson
	Skelly, George A.	St. Paul
	Skinner, Abbott	St. Paul
†	Skinner, Harvey O.	St. Paul
#	Skinner, Ira C., III	San Antonio, TX
	Skjold, Arthur C.	Minneapolis
	Skogerboe, Rudolph	Grand Forks
	Skumatz, Primus J., Jr.	International Falls
	Slack, William J.	Duluth
	Slanga, Roger A.	St. Cloud
	Slater, Edward J.	Bemidji
	Sletten, Richard G.	Minneapolis
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	Slosser, Gaius J.	Minneapolis
	Smeby, Loren A.	Minneapolis
	Smelker, Jean	Minneapolis
£	Smigiel, Mitchell R., Jr.	Rochester
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	Smiley, John T.	Minneapolis
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£	Smisek, Frank M.	Minneapolis
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	Smith, Archie M.	Minneapolis
	Smith, Barlow	Edina
	Smith, Baxter A., Jr.	Minneapolis
	Smith, Cyril M.	Duluth
	Smith, George R.	Hutchinson
	Smith, Graham G.	Minneapolis
	Smith, H. Nippert	St. Paul
	Smith, Harry J.	Lake Crystal
	Smith, Henry T.	Minneapolis
£	Smith, James C.	St. Paul
	Smith, James M.	Minneapolis
	Smith, John E.	Minneapolis
	Smith, J. Weston	St. Cloud
	Smith, Lucian A.	Rochester
	Smith, Nadine G.	Minneapolis
	Smith, Ralph E.	Rochester

	Smith, Theodore S.	Minneapolis
	Smith, Vernon D. E.	St. Paul
	Smith, Wallace R.	Grand Marais
	Smith, William T.	St. Paul
	Smookler, Richard A.	St. Paul
	Smorstok, Matthew B.	Monticello
	Smyth, John J.	Lester Prairie
†	Smythe, Gwendolyn S.	Austin
	Smythe, Lowell J.	Austin
	Snider, Howard R.	Mankato
	Snyder, Clinton F.	Austin
†	Snyder, George W.	St. Paul
	Snyder, Robert E.	Spring Valley
	Soderberg, Richard J.	Minneapolis
†	Soderlind, Ragnar T.	Minneapolis
†	Sohlberg, Olof I.	St. Paul
	Soiseth, Robert P.	Minneapolis
	Solhaug, Michael J.	Minneapolis
	Solhaug, Samuel B., Jr.	Minneapolis
	Solien, Arylo	Parkers Prairie
	Solvason, Harold M.	Minneapolis
£	Somerville, Gordon W.	Rochester
	Sommer, R. K.	Elk River
	Sommerdorf, Stephen D.	St. Cloud
	Sommerdorf, Vernon L.	St. Paul
	Sommers, Stephen D.	St. Cloud
	Sondreal, Wesley D.	Bemidji
	Sonnesyn, Nels N.	Le Sueur
	Sontag, David W.	Lake City
	Soriano, Dominador B.	Onamia
	Saucheray, John A.	St. Paul
	Soukup, Dennis A.	Duluth
	Soule, Edward H.	Rochester
†	Souster, Benjamin B.	St. Paul
	Sowada, Dorothea P.	St. Paul
	Sowada, Ernest J.	St. Paul
	Spagnolo, Anthony A.	Shakopee
†	Spang, Anthony J.	Duluth
†	Spang, James S.	Duluth
	Spang, William M.	Duluth
	Spangler, Maurice W.	Park Rapids
	Spano, Joseph P.	Minneapolis
	Speckhals, Robert C.	Faribault
	Spencer, Bernard J.	Minneapolis
	Spencer, David L.	Minneapolis
	Spencer, Joseph F.	Duluth
	Spencer, Robert J.	Rochester
	Spenny, Edward A. L.	Minneapolis
	Sperl, Michael P., Jr.	St. Paul
	Sperling, Keith B.	Minneapolis
	Spiekerman, Ralph E.	Rochester
	Spieler, Forrest B.	Pequot Lakes
	Spilseth, Paul	Stillwater
	Spink, Wesley W.	Minneapolis
	Spittell, John A., Jr.	Rochester
	Sponsel, Kenath H.	Minneapolis
	Sprafka, Gregory A.	St. Paul
	Sprafka, Joseph L.	St. Paul
†	Sprague, Randall G.	Rochester
	Spraitz, Anton F., Jr.	St. Paul
£	Springrose, James V.	Minneapolis
†	Spurzem, Raymond J.	Anoka
£	Sridaromont, Somkid	Rochester
	Stadem, Clifford J.	Crookston
	Stafne, John G.	St. Paul
	Stahl, George W.	Austin
	Stahler, Paul A.	Jordan
	Stahn, Louis H.	St. Cloud
	Stahr, Aubrey C.	Hopkins
	Stam, John	Worthington
	Standefer, James E.	Stillwater
†	Stanford, Charles E.	Elcho, WI
	Stansbury, John A.	Minneapolis
†	Stauffer, Maurice H.	Rochester
	Steidl, Richard M.	Minneapolis
†	Stein, Raymond J.	Pierz
	Steinberg, Charles L.	St. Paul
	Steiner, Andrew M.	St. Michael
	Steiner, Leon E.	Albert Lea
	Steinhilber, Richard M.	Rochester
†	Stelter, Lloyd A.	Minneapolis
	Stemsrud, Harold L.	Alexandria
†	Stenstrom, Annette T.	Grand Marais
	Stenwick, Michael W.	Minneapolis
	Stenzel, Donald A.	Minneapolis
	Stenzel, Joseph A.	Minneapolis
	Stephens, David H.	Rochester
	Stephens, William E.	Minneapolis
	Sterner, Donald C.	St. Paul
	Sterner, John J.	St. Paul
	Sterrie, Norman A.	Minneapolis
	Stevens, Sheridan S. H.	Minneapolis
£	Stevenson, Edward K.	Rochester
	Stewart, Donald E.	Crookston
	Stewart, John W.	Duluth
	Stewart, Marvin J.	Minneapolis
	Stewart, Paul B.	Minneapolis
	Stewart, Richard O.	Winona
	Stickler, Gunnar B.	Rochester
	Stickney, J. M.	Rochester
	Stiegler, Farrell S.	Minneapolis
	Stiles, Clifford D.	Foley
£	Stillman, M. Thomas	Minneapolis
	Stillwell, George K.	Rochester
†	Stillwell, Walter C.	Mankato
†	Stilwell, George G.	Rochester
	Stock, John F.	Morris
	Stoker, Lynn C.	Albert Lea
	Stolee, Curtis N.	Le Sueur
	Stolee, Thomas A.	St. Paul
	Stolen, Keith H.	Grand Rapids
	Stoltz, Robert C.	Minneapolis
	Stone, Norman F.	Minneapolis
	Stone, Stanley P.	Minneapolis
£	Stone, Stephen P.	Rochester
	Stonnington, Henry H.	Rochester
	Storsteen, Kenneth A.	Duluth
	Stover, Laddie E.	Marshall
	Stoy, Robert A.	Little Falls
	Strait, Herbert S.	Minneapolis
	Strand, Clarence M.	Minneapolis
	Stack, John F.	Morris
	Strand, Jack W.	Jasper
	Strand, Peter J.	Minneapolis
	Strand, Richard C.	Bloomington
	Strand, Roger W.	Willmar
	Stransky, Theodore W.	Owatonna
	Strate, Richard G.	St. Paul
	Strathern, Carleton S.	St. Peter
†	Stratte, Alf K.	Pine City
†	Stratte, Harold C.	Windom
	Stratte, Jon R.	Stillwater
	Strauchler, John	Belview
	Straus, Maurice L.	St. Paul
	Street, Bernard	Northfield
	Streitz, John M.	Duluth
	Strem, Edward L.	St. Paul

	Streu, Richard E.	Minneapolis
	Strewler, Gordon J.	Duluth
	Strickler, Jacob H.	Minneapolis
§	Stringer, Gene C.	St. Paul
	Strobel, Jack L.	Minneapolis
†	Stroebel, Charles F., Jr.	Rochester
	Strom, Gordon W.	Minneapolis
	Strom, Robert L.	Minneapolis
	Stromgren, Delph T.	Minneapolis
	Stromme, William B.	Minneapolis
	Strong, Cameron G.	Rochester
	Strough, LaVern C.	Worthington
	Strouth, Jonas C.	Virginia
*	Strunk, Clarence A.	Minneapolis
	Struthers, Lewis E.	Parkers Prairie
	Stubbs, Samuel E.	Rochester
	Student, Richard E.	Minneapolis
	Studer, Donald J.	Faribault
	Sturgeon, Richard R.	Minneapolis
	Sturges, Robert L.	Minneapolis
	Sturley, Rodney F.	St. Paul
	Subak, Barbara H.	Minneapolis
	Subby, Walter	Minneapolis
£	Suh, Ku Won	Rochester
†	Sukov, Marvin	Minneapolis
	Sulciner, Aurel	Minnetonka
£	Sullivan, Cornelius	St. Paul
	Sullivan, W. Albert, Jr.	St. Paul
	Summar, M. Thomas	Fridley
	Summerskill, William H.	Rochester
	Sundberg, A. Bruce	Minneapolis
	Sundt, Thoralf M., Jr.	Rochester
£	Sung, David T. W.	Rochester
	Sutherland, John E.	Indian Head, MD
	Swaiman, Kenneth F.	Minneapolis
	Swallen, Thomas O.	Minneapolis
	Swanson, David A.	Edina
	Swanson, David W.	Rochester
	Swanson, Gerald E.	Minneapolis
£	Swanson, Gene E.	Rochester
	Swanson, John O.	Minneapolis
	Swanson, Lawrence J.	West St. Paul
	Swanson, Ralph H.	West St. Paul
#	Swanson, Wallace L.	Quito Ecuador, S.A.
	Swayze, Claude R.	St. Paul
	Swedberg, William A.	Duluth
†	Swedenburg, Paul A.	Glenwood
†	Sweetser, Horatio B.	Minneapolis
	Sweetser, Theodore H., Jr.	Minneapolis
	Swendseen, Carl J.	Minneapolis
†	Swendson, James J.	St. Paul
	Swensen, Don P.	Duluth
†	Swenson, Arnold O.	Ft. Myers, FL
	Swenson, Donald B.	St. Paul
	Swenson, Donald B.	Mankato
	Swenson, Floyd J.	Minnetonka
	Swenson, James D.	Edina
	Swenson, Orville P.	Cloquet
	Swenson, Richard W.	Minneapolis
†	Swenson, Roy G.	North Branch
	Swift, Dean C.	Minneapolis
#	Swint, Robert E.	29 Palms, CA
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	Symchych, Boris E.	Minneapolis
	Syverson, Leslie A.	Fergus Falls

T

	Taddeini, Luigi	St. Paul
	Tagatz, George E.	Minneapolis
	Taintor, Ronald W.	Marshall
	Talsness, Jon M.	International Falls
	Tam, Ernest C.	Minneapolis
	Tambornino, Joseph M.	Minneapolis
	Tan, Ruby	Marshall
	Tanaka, Shin	Minneapolis
	Tanasichuk, Murray A.	St. Paul
#	Tangedahl, Tim N.	Bismarck, ND
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	Tani, George T.	St. Paul
†	Tanquist, Edwin J.	Alexandria
	Tanquist, Edwin J., Jr.	Alexandria
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£	Taylor, Ross M.	Thief River Falls
	Tchou, Mien-Fa	Minneapolis
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	Telander, Robert L.	Minneapolis
	Tempel, J. W.	Blue Earth
	ten Bensel, Robert J.	Minneapolis
	Tenner, Robert J.	Minneapolis
	Terrell, Bernard J.	Mt. Vernon, MD
	Tesch, Gordon H.	Elk River
	Teska, Byron A.	Minneapolis
	Testor, James V.	Winona
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	Teynor, Joseph W.	Minneapolis
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	Thienes, R. Lawrence	St. Cloud
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	Thomasson, Robert D.	Minneapolis
	Thomas, A. Boyd	Minneapolis
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	Thompson, Arthur	Minneapolis
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¶	Thompson, Conrad O.	Rochester
	Thompson, Carl O.	Hendricks
†	Thompson, Gershom J.	Rochester
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†	Thomson, James	St. Paul
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	Thorsgard, Ernest O.	Thief River Falls
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	Thorson, Stuart V.	Minneapolis
£	Throckmorton, Tom D.	Rochester

	Thurber, Deloran L.	Rochester
	Thuringer, Carl B.	St. Cloud
	Thurn, Roy J.	Duluth
	Thysell, Vernon D.	Moorhead
	Tiede, James J.	Willmar
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	Tifft, Cyril R.	St. Paul
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	Tinkham, Robert G.	Rochester
£	Tinstman, Thomas C.	Rochester
	Titrud, Leonard A.	Minneapolis
	Tiu, Ofelio D.	Fridley
	Tobin, John A.	Minneapolis
	Tobin, John D.	Minneapolis
	Todd, John C.	Austin
	Tombers, Joseph M.	Minneapolis
	Tompkins, Richard B.	Rochester
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	Torres, Fernando	Minneapolis
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	Townes, C. Dwight, Jr.	Minneapolis
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	Treanor, Thomas A.	Albert Lea
	Tregilgas, Richard B.	St. Paul
	Trost, Francis J.	Minneapolis
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	Troup, Elliott V.	St. Paul
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	Trow, William H.	St. Paul
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	Tsai, Shih Hao	Minneapolis
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	Tuason, Vincente	St. Paul
	Tucker, Richard C.	Minneapolis
	Tudor, Richard B.	Minneapolis
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	Tuma, Benjamin M.	Faribault
	Turbak, Charles E.	Minneapolis
	Turkbas, Nejat	Minneapolis
	Tveten, Omar A.	St. Paul
	Tweedy, John A.	Winona
	Tweedy, Robert	Winona
	Twidwell, Joseph E.	Minneapolis
	Twiggs, Leo F.	Austin
	Tyce, Francis A.	Rochester
	Tygart, Robert L.	Duluth

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†	Uihlein, Alfred	Rochester
	Ulrich, Emery E.	Duluth
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	Ulvestad, Harold S.	Minneapolis
	Undem, Dale	Alexandria
	Underdahl, L. O.	Rochester
	Urganyi, Eugene W.	St. Cloud
	Utendorfer, Robert W.	Minneapolis
	Utz, David C.	Rochester

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	Vaaler, Robert T.	Minneapolis
	Vaccarella, R. James	St. Paul
	Valgemae, Romil	Minneapolis
	Van Bergen, Frederick H.	Minneapolis
	Van Cleve, Horatio P., Jr.	Austin
	Van DeRiet, Lowell W.	St. Paul
	Vanderpool, Thomas E.	Paynesville
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